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P493 ORAL-ATO/ATRA/ASCORBIC ACID (AAA)-BASED INDUCTION OR MAINTENANCE OF FIRST COMPLETE REMISSION IMPROVED OUTCOMES IN NEWLY DIAGNOSED APL: A MULTICENTRE ANALYSIS OF THE APL ASIAN CONSORTIUM (APLAC)

Topic: 4. Acute myeloid leukemia - Clinical

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Background:

Pure oral arsenic trioxide (oral-ATO) solution (Arsenol ®) was first formulated in Hong Kong. It achieves a bioavailability comparable to that of intravenous ATO (i.v.-ATO). Oral-ATO, used in combination with all trans retinoic acid (ATRA) and ascorbic acid (the AAA regimen) has been shown to highly effective in re-induction of relapsed acute promyelocytic leukaemia (APL), and in the frontline induction, consolidation and maintenance of newly-diagnosed APL. However, the relative outcomes of APL treated with regimens based on ATRA/chemotherapy, i.v.-ATO/ATRA, and oral-ATO/ATRA have not been critically appraised.

Aims:

The objectives of this multicentre retrospective cohort analysis were: 1. to define the clinicopathologic features of APL in Asia; 2. to compare the outcomes in newly-diagnosed APL treated with regimens based on ATRA/chemotherapy, i.v.-ATO/ATRA, and oral-ATO/ATRA/ascorbic acid (AAA).

Methods:

Patients with newly-diagnosed APL treated in 14 centres (Hong Kong:9; Taipei: 1; Thailand: 1; Singapore: 1; Malaysia: 2) between 1 January 2001 to 30 July 2022 were identified. Information on the clinicopathologic features, treatment and outcomes were collected. Primary outcomes were 60-day survival (time from presentation to death, censoring at day 60), overall survival (OS, time from presentation to death or last follow-up), and relapse-free survival (RFS, time from first complete remission, CR1, to relapse, death or last follow-up). Data were censored on August 30, 2022. Survivals (60-day survival, OS, RFS) were analyzed with the Kaplan-Meier method, difference between groups determined with the log-rank test and Cox proportional hazard model.

Results:

There were 334 men and 332 women at a median age of 44 (range: 3-91) years, with 460 patients (69.1%) in the standard-risk (presenting leucocyte ≤ 10 x 10^9/L) and 206 patients (30.9%) in the high-risk (presenting leucocyte > 10 x 10^9/L) groups. According to induction/consolidation/maintenance regimens, patients were divided into four groups: ATRA/chemotherapy based induction/consolidation/maintenance, N=324; ATRA/chemotherapy based induction/consolidation + AAA maintenance, N=127; i.v.-ATO/ATRA-based induction/consolidation, N=61; and AAA-based induction/consolidation/maintenance, N=154. Notably, 49% of patients did not receive ATO because of drug access problems. After a median follow-up of 74.5 months (interquartile range: 29-132 months), there were

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112 deaths (16.8%). The 60-day survival was 91.6%. On multivariate analysis, inferior 60-day survival was associated with age > 50 years (P=0.02), central nervous system (CNS) involvement at presentation (P<0.001) and non-ATO (oral or i.v.)-based induction (P<0.001). The 5-year OS was 87%. On multivariate analysis, inferior OS was associated with age > 50 years (P=0.001), CNS involvement at presentation (P<0.001) and APL differentiation syndrome (DS) (P<0.001); and the use of ATRA/chemotherapy-based induction/consolidation and CR1 AAA maintenance (5-year OS: 93.5%; P=0.04) and AAA-based induction/consolidation/maintenance (5-year OS: 92.4%; P=0.002). . The 5-year RFS was 82.4%. On multivariate analysis, inferior RFS was associated with male sex (P=0.04) and CNS involvement at presentation (P<0.001); and the use of i.v.-ATO/ATRA-based induction/consolidation (5-years RFS: 92.8%; P=0.005), ATRA/chemotherapy-based induction/consolidation and CR1 AAA maintenance (5-year RFS: 88%; P<0.001), and AAA-based induction/consolidation/maintenance (5-year RFS: 97.8%; P<0.001).

Summary/Conclusion:

The use of AAA-based regimens in newly-diagnosed APL significantly improved early deaths, OS and RFS independent of conventional risk grouping.

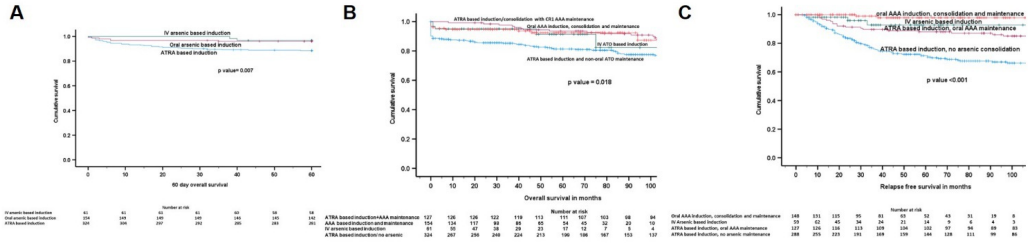

Figure. Survivals of patients with newly-diagnosed acute promyelocytic leukaemia (APL) in the APL Asian Consortium. A: 60-day survival; B: Overall survival of 4 different induction/consolidation/maintenance regimens; C: Relapse-free survival of 4 different induction/consolidation/maintenance regimens.