Abstract: S102

Title: FIRST RESULTS OF THE APOLLO TRIAL: A RANDOMIZED PHASE III STUDY TO COMPARE ATO COMBINED WITH ATRA VERSUS STANDARD AIDA REGIMEN FOR PATIENTS WITH NEWLY DIAGNOSED, HIGH-RISK ACUTE PROMYELOCYTIC LEUKEMIA

Abstract Type: Oral Presentation

Session Title: Plenary Abstracts Session

Background:

Pioneered by the APL0406 trial (Lo-Coco et al., NEJM 2013), prior investigations have demonstrated the superiority of combining all-trans retinoic acid (ATRA) and arsenic trioxide (ATO) over standard ATRA and chemotherapy (CHT) as front-line management of low/intermediate risk acute promyelocytic leukemia (APL). However, the efficacy of ATRA/ATO in high-risk APL (HR-APL), defined as >109/L white blood cell counts (WBC) at diagnosis, has not been studied within randomized trials so far.

Aims:

The objective of the APOLLO trial was to prospectively compare the efficacy of the ATRA-ATO regimen (arm A) versus the standard of care (ATRA-CHT; arm B) in patients with HR-APL.

Methods:

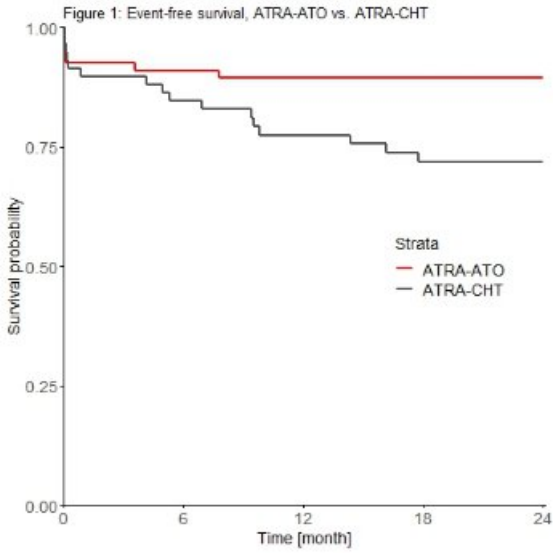
The APOLLO trial (NCT0268840) is an open-label, randomized European intergroup trial. Eligible pts are aged 18-65 years with newly diagnosed HR-APL. Patients in the ATRA-ATO arm received two doses of idarabucin (12 mg/m2) on day 1 and 3, plus ATO 0.15 mg/kg and ATRA 45 mg/m2, daily until CR. Consolidation consisted of 4 courses of ATO 5 days/week, 4 weeks on 4 weeks off, for a total of 4 courses, in parallel with ATRA 2 weeks on and 2 weeks off (7 courses). Patients in the ATRA-CHT arm received the standard AIDA (ATRA+Idarubicin) induction followed by 3 cycles of CHT-based consolidation as well as maintenance. The primary study endpoint is EFS at 2 years including the following events: no achievement of CR after induction therapy; no achievement of molecular remission after consolidation; relapse (hematological/molecular); death including early death or development of secondary myelodysplasia or leukemia. Secondary endpoints include overall survival (OS), toxicity, measurable residual disease and quality of life assessments. ATO was provided free of charge by TEVA pharmaceuticals. The project was funded by the German Federal Ministry of Education and Research.

Results:

The study was prematurely discontinued in August 2022, due to slow recruitment during the Covid-19 pandemic, and expiration of study-drug reserved for the trial. Maintenance treatment and observational period are still ongoing. Overall, 131 patients are evaluable for outcome, 68 in Arm A and 63 in arm B. Median WBC was 36 x109/L (10.1-489.0 x109/L) and 39% had WBC > 50 x109/L. CR+CRi was achieved in 63/68 (93%) in the ATRA-ATO *versus* (*vs*) 57/63 (91 %) in the ATRA-CHT arm (P= 0.65). Early death rate was similar across arms (5 and 7 pts in the ATRA-ATO and ATRA-CHT arm, respectively). Causes of early death were bleeding in 3 and 4, sepsis in 0 and 2, thrombosis in 1 and 1, pulmonary failure due to leucostasis related to APL in 1 and 0 pts in the ATRA-ATO and ATRA-CHT arm, respectively. A total of 120 out of 131 patients are currently evaluable for disease status following induction. After a median follow-up of 31 months (range 1.7 – 71.5 months), the 2-year EFS was 89% and 72% in the ATRA-ATO and ATRA-CHT groups respectively (P= 0.02, Figure 1). Molecular relapse was observed in 0 and 6 pts in the ATRA-ATO and ATRA-CHT arm, respectively. The 2-year OS rate was 93% *vs* 87% (P= 0.33) for ATRA-ATO vs ATRA-CHT, respectively. Death in CR/CRi were observed in 0 and 3 pts in the ATRA-ATO and ATRA-CHT arm, respectively. Analysis of safety is ongoing.

Summary/Conclusion:

First-line therapy with ATRA-ATO with two initial doses idarubicin results in superior EFS compared to conventional ATRA-CHT in patients with HR-APL. Further analysis of the APOLLO trial may support the implementation of this regimen as the new standard of care in patients with HR-APL.



Keywords: Acute myeloid leukemia, Acute promyelocytic leukemia, ALL-trans retinoic acid (ATRA), Arsenic trioxide