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S136 ANALYSIS OF FACTORS ASSOCIATED WITH LONG-TERM SURVIVAL IN A LARGE ACUTE PROMYELOCYTIC LEUKEMIA (APL) PATIENT COHORT: A HARMONY ALLIANCE STUDY

Topic: AML clinical studies and risk stratification

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Background:

APL, once regarded as the most rapidly fatal acute myeloid leukemia (AML), is now curable in 75-90% of patients using targeted agents [All-trans retinoic acid (ATRA)+Arsenic Trioxide (ATO)] or ATRA combined with chemotherapy (ATRA+Idarubicin, AIDA-based). The large HARMONY registry offered the opportunity to merge APL patient populations enrolled in clinical trials or treated in the real life to address open issues in the disease management.

Aims:

Long-term follow-up of a large patient cohort diagnosed with APL and treated in 2 European trials (UK AML-17 and GIMEMA APL0406) as well as national registries from 6 countries.

Methods:

The Harmony platform includes to-date 1868 patients, newly diagnosed with APL in the years 2007-2020. The list of variables includes: age, gender, year of diagnosis, Sanz Risk-group, FLT3-ITD mutation status, Bcr subtype, secondary vs de novo APL, rate of differentiation syndrome and role of intra-thecal prophylaxys, rate of relapse or death from any causes. The present analysis was carried out in 674 patients, who underwent treatment and met the data quality requirements. These patients were treated according to APL0406 and AML17 clinical trials, or were included in the Study Alliance Leukemia (SAL) national registry. After acquisition from the sources, data were harmonized and transformed using an Observational Medical Outcomes Partnership Common Data Model, and eventually registered in the HARMONY Big Data Platform.

Results:

Of 674 patients, 320 were treated with ATRA-ATO (median age 48.5 years, range 16-87; 47.8% female), and 354 with ATRA-Idarubicin (AIDA, median age 47 years, range 17-82; 51.1% female). According to Sanz risk-score, in the ATRA-ATO cohort, 141 patients (44%) were low risk (LR), 144 (45%) intermediate risk (IR), and 31 (10%) high risk (HR, data not available in 4 patients, 1%). The AIDA cohort included 116 (33%) LR, 153 (43%) IR, and 78 (22%) HR patients, while data were not available in 7 patients (2%). The 10-year overall survival (OS) rate

was 92% and 85%, in ATRA-ATO vs AIDA groups, respectively (p=0.024, figure 1). At a median follow-up of 5.67 years (range 0.03-10.25), OS in patients treated with ATRA-ATO was similar in the Sanz-risk classes (LR: 93%, IR: 92%, HR: 87%, p=0.139). The median follow-up of patients treated with AIDA was 5.88 years (range: 0-14.2), while survival was 93% in LR, 84% in IR, and 76% in HR APL (p=0.05). Survival was significantly associated with age (<60 years n=523, 61-70 n=111, 71-80 n=37, >80 n=3), both overall (p<0.001) and in patients grouped for treatment (ATRA-ATO: p<0.001, AIDA: p=0.087). There were no significant differences in the rate of early deaths (<day 30 from diagnosis) between the two groups (2.8% vs 3.1%, respectively). Patients treated in the real life had inferior survival when compared to clinical trials, both in the AIDA cohort (7-year OS: 69% vs 89%, p=0.003) and in the ATRA-ATO cohort (7-year OS: 88% vs 95%, p=0.058) and a similar rate of early deaths (4.4% vs 2.8%).

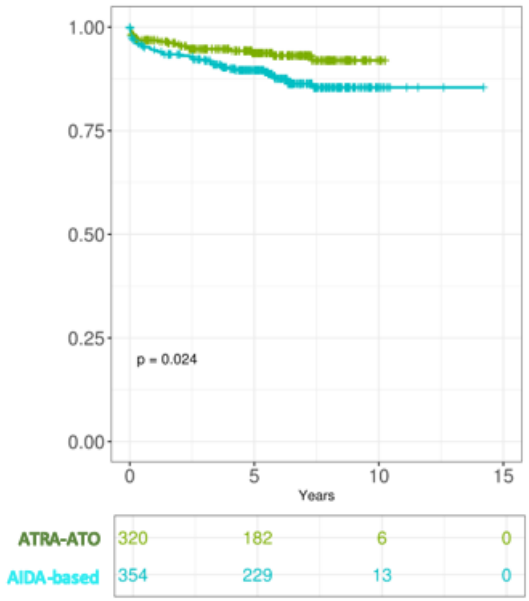

Figure 1. Survival analysis in newly diagnosed Acute Promyelocytic Leukemia patients receiving ATRA-ATO vs AIDA-based treatment.

Summary/Conclusion:

This first analysis on the Harmony APL project shows a significant survival advantage of patients treated with the ATRA-ATO chemo-free regimen at 10 year-follow-up, irrespective of the Sanz-risk score. The latter maintains its prognostic relevance in patients treated with the AIDA regimen. Age resulted significantly associated with OS, irrespective of treatment. Patients enrolled in clinical trials presented improved survival both in AIDA and in ATRA-ATO cohorts.