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POSTER ABSTRACTS

617.ACUTE MYELOID LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS

Feasibility and Relevance of Incorporating Genetic Testing By Next-Generation Sequencing for Acute Myeloid Leukemia Patients Treated in Low- and Middle-Income Countries

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Background: The outcome of the treatment for acute myeloid leukemia (AML) in low- and middle-income countries (LMIC) is significantly worse than in high-income ones due to several factors, including higher non-relapse mortality from infections and limited access to hematopoietic stem-cell transplantation (HSCT). In this resource-constrained setting, AML-risk stratification is based exclusively on cytogenetics, which has longer turn-around time and higher failure rates compared to next-generation sequencing (NGS). Here, we report the benefit of adding a simplified NGS gene panel to improve risk stratification for 279 adult Brazilian patients with AML (male=146, female=136; mean age=50 years; range 18-65) included in International Consortium of Acute Leukemia (ICAL) 2015 Study. **Material & Methods:** Samples from 10 ICAL centers were shipped to the National Central Lab at the University of São Paulo at Ribeirão Preto Medical School, Brazil (located zero to 1420 kilometers from centers). All patient samples were assessed by conventional cytogenetics and molecular tests by RT-PCR for *RUNX1::RUNX1T1* and *CBFB::MYH11* , PCR and fragment analysis for *NPM1* and *FLT3*-ITD allelic ratio, and Skyline AML profiler assay for *CEBPA* double mutant. We retrospectively searched for mutations in the *ASXL1, CEBPA, FLT3, IDH1, IDH2, NPM1, RUNX1, TP53* genes using NGS in 53 out of the 279 samples. The tests were performed in the Illumina iSeq100 Sequencing System using reagents and methodology developed under the supervision of the Erasmus MC Cancer Institute (Valk Laboratory) as part of the activities of the ICAL Laboratory Subcommittee. Training, including bioinformatics analysis, was provided virtually and through a short-term visiting program (ASH Visitor Training Program) to Erasmus MC. Datasets with genetic testing results obtained locally were sent and reanalyzed at Erasmus MC and discussed in bi-monthly meetings. Risk stratification was determined either by cytogenetics only or by cytogenetic and molecular analysis according to the ELN 2017 proposal. Overall survival (OS) was defined from date of diagnosis to last follow up or death and compared by Kaplan-Meier and Log-Rank test followed by Benjamini-Hochberg *p*-value adjustment method, using R 4.3.1. **Results:** conventional cytogenetics was informa-

tive in 68% (190/279) of the cases, and based on those results 32 (16.8%), 116 (61%) and 42 (22.1%) patients were stratified into favorable, intermediate and adverse categories, respectively. However, no significant difference in the OS was detected according to cytogenetic risk. When genetic testing by NGS was added, 54 (27.3%), 98 (49.5%) and 46 (23.2%) patients were assigned into favorable, intermediate and adverse categories, respectively. Twenty-six (48%) patients had risk re-classified as a consequence of the NGS results. Moreover, two out of four patients whose risk stratification could not be assigned due to insufficient metaphasis were classified based on NGS results. Of note, the median OS of the favorable group was significantly longer (not reached) than that of intermediate and of the adverse groups (6 months), ($p<0.0001$), but no difference was detected between the latter two. We also assessed whether genetic testing by NGS would change the risk category of AML patients previously classified based on conventional cytogenetics in association with the evaluation of gene rearrangements, *NPM1*, *FLT3* and *CEBPA* mutational analysis by methods other than NGS. NGS results changed the category of 3 out of 54 patients. Our results indicate the feasibility of developing a simplified platform of genetic testing for AML based on NGS in LMIC, which was able to improve the identification of favorable-risk patients and may help to better allocate resources.

Disclosures Traina: *Novartis:* Consultancy. **Duarte:** *Astrazeneca:* Speakers Bureau. **Silva:** *Servier:* Honoraria; *Pfizer:* Honoraria; *Libbs:* Research Funding. **Haferlach:** *MLL Munich Leukemia Laboratory:* Current Employment, Other: Equity Ownership. **Rego:** *Abbvie:* Honoraria, Speakers Bureau; *Astellas:* Research Funding, Speakers Bureau; *Pfizer:* Honoraria, Research Funding.

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