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# POSTER ABSTRACTS

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

### Early Peripheral Blood Blast Clearance As a Prognostic Marker for Early Treatment Response in Pediatric Acute Myeloid Leukemia

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**Background and Significance**

The cure rate of pediatric acute myeloid leukemia (AML) has improved significantly; however, relapses still occur in up to 30% of the total patient population in high-income countries (HICs), and in an even higher percentage of patients in low- and middle-income countries (LMICs). Early treatment response, cytogenetics and minimal residual disease (MRD) are well-known prognostic factors for treatment outcome; however, sophisticated techniques for identifying prognostic factors are often lacking in LMICs, and are sometimes unsuccessful in HICs. Early treatment response assessed by a bone marrow (BM) aspirate on day 15 or day 22 (D22) (depending on the applicable protocol) after initiation of chemotherapy is a known prognostic factor for outcome in patients with pediatric AML, but does not allow modifications of the first induction chemotherapy course (Creutzig 2014, Abrahamsson 2011, Kern 2003). In both pediatric acute lymphoid leukemia (ALL) and adult AML, early peripheral blood blast clearance (PBBC) is a known early indicator of treatment response (Manabe 2008, Arellano 2012), whereas to the best of our knowledge, this has not yet been reported in pediatric AML. In this study, we evaluated the significance of time to complete PBBC, and rate of PBBC after initiation of chemotherapy, in relation to disease status in BM D22, as measure of early treatment response that has prognostic significance.

**Study Design and Methods**

Pediatric patients with AML, aged 0-18 years, that were treated according to the NOPHO-DBH AML-2012 protocol were included. The first 5 days of induction therapy consisted of etoposide, followed by 7 days of low-dose cytarabine and mitoxantrone or liposomal daunorubicin. Peripheral blood (PB) was assessed by morphology at the time of diagnosis, daily in the first week, and thrice weekly until D22 or until occurrence of complete clearance of blasts. BM D22 was assessed by morphology and flow cytometry. A receiver operating characteristic (ROC) analysis was performed to evaluate the predictive power of days from starting chemotherapy to complete PBBC. The correlation between time to complete PBBC and BM D22 results was analyzed using a logistic regression model. Multivariable logistic regression models were applied for the association after adjusting for effects of other covariates. Rate of PBBC was defined as the percentage of the absolute PB blast count on the day of diagnosis that cleared with each day of therapy, on average, until D22 or the day of complete PBBC.

**Results**

In total, 319 patients were included, out of whom 241 were eligible for analysis, and 78 not eligible due to missing or incomplete data. Day 9 after initiation of chemotherapy was identified as the most discriminating cut-off point for predicting BM D22 response. Patients were categorized into early PBBC (≤9 days; n=159) and delayed PBBC (>9 days; n=82) groups. Early PBBC was associated with having <5% AML cells in BM D22 as assessed by both morphology (OR 3.11; P=0.005) and flow cytometry (OR 2.73; P=0.041). Early PBBC also showed a much lower likelihood of having >15% AML cells in BM D22 by morphology (OR 0.08; P=0.002). None of the early PBBC patients had >15% AML cells in BM D22 by flow cytometry. For

217 patients (selection due to missing data [n=24]), the rate of PBBC could be calculated, and a discriminative cut-off value of 11% was identified. Patients were categorized into high rate of PBBC (>11%; n=132) and low rate of PBBC (≤11%; n=85). High rate of PBBC was associated with having <5% AML cells in BM D22 by flow cytometry (OR 4.30; P=0.007) and negative MRD status (OR 2.02; P=0.004), while also showing a strong association with a lower likelihood of >15% AML cells in BM D22 (OR 0.11; P=0.007) by morphology. None of the high rate PBBC patients had >15% AML cells in BM D22 by flow cytometry.

**Conclusion**

Both early complete PBBC and rate of PBBC after initiation of chemotherapy holds promise as prognostic marker for clinical outcome in pediatric AML, as it correlates significantly with BM D22 response. These findings may offer an early and easily accessible prognostic factor, particularly beneficial for LMICs, as well as for patients with unsuccessful MRD analyses.

**Disclosures** No relevant conflicts of interest to declare.

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