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ABSTRACTS

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Free Contributions

Poster Session

CLINICAL STUDIES IN AML AND ALL (P001–P025)

P001. Survival analysis of GIMEMA AML1718, a Safety Run-in and Phase 2 Open-Label Study of Venetoclax, Fludarabine, Idarubicin and Cytarabine (V-FLAI) in the Induction Therapy of non Low-Risk Acute Myeloid Leukemia

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Background: Despite therapeutic advances, the prognosis for intermediate- and high-risk acute myeloid leukemia (AML) remains poor, with an estimated 2-year overall survival (OS) of 30–40% in younger patients. The GIMEMA AML1718 trial investigated the combination of venetoclax with fludarabine, idarubicin, and cytarabine (V-FLAI) as induction therapy to improve outcomes for these patients. Primary endpoint analysis demonstrated a high rate of complete remission (CR) and measurable residual disease (MRD) negativity (79% and 64%, respectively). Here, we present mature data on overall survival (OS) and disease-free survival (DFS).
Methods: The GIMEMA AML1718 trial (NCT03455504) is a Phase 1/2 multicenter study that enrolled newly diagnosed adult patients with ELN 2017 intermediate- or high-risk AML. The trial followed a modified Simon's two-stage design. Safety was established in a run-in phase with venetoclax dosages of 400 mg or 600 mg, with no significant difference between the dosages. Part 2 included 67 patients treated with 400 mg V-FLAI. Induction cycles and consolidation treatments were tailored, with allogeneic hematopoietic stem cell transplantation (HSCT) performed when feasible. MRD was centrally assessed in Part 2. A 91-gene panel is under investigation for further characterization of patients.
Results: A total of 124 patients were enrolled, with a median age of 55 years (range 18–66), 56% male. At baseline, 54% were classified as intermediate risk, and 46% as high-risk, primarily based on cytogenetics and FLT3/NPM1 status. FLT3 mutations were present in 15.3% of patients, while 14% had secondary AML. After induction, 74 patients (59.6%) proceeded to consolidation, and 71 (57.2%) received HSCT (93% in first CR). With a median follow-up of 22 months, the 1- and 2-year OS were 61% and 48%, respectively, while DFS was 60% and 46%. The survival curves suggest a plateau after 2 years, with 48% of longterm survivals (figure). Safety analysis confirmed low treatment-related mortality (4%) and no severe late effects, graft failures, or elevated incidence of graft-versus-host disease.
Conclusions: V-FLAI demonstrates durable survival benefits in intermediate- and high-risk AML, with a favorable safety profile. These results suggest that V-FLAI may be a superior induction strategy for fit, non-low-risk AML patients, supporting the need for randomized trials comparing it to standard of care.
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MINIMAL RESIDUAL DISEASE (P052–P062)

P052. Retrospective validation of computational measurable residual disease assessment in acute myeloid leukemia in the HOVON-SAKK-132 trial

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Introduction: Flow cytometry is recommended for measurable residual disease (MRD) assessment in acute myeloid leukemia (AML). While flow cytometry is widely applicable and cost-effective, manual gating-based MRD (mgMRD) analysis is time-consuming (~30 minutes per sample) and faces challenges in consistency and standardization, particularly in resource-limited settings. To address these issues, we previously developed a fast (~3 seconds) and interpretable computational MRD (cMRD) pipeline using machine learning. This algorithm first automatically detects healthy and leukemic immature myeloid cells, after which a statistical model detects and quantifies cells with aberrant marker expression.

Methods: To assess the prognostic relevance of cMRD, we retrospectively analyzed the HOVON-SAKK132 trial using our pipeline. cMRD assessment was performed for all bone marrow aspirates collected from AML patients in remission after two cycles of chemotherapy measured at the central laboratory at Amsterdam UMC according to MRD guidelines. Survival outcomes were evaluated based on overall survival (OS), relapse-free survival (RFS), and cumulative incidence of relapse (CIR).

Results: We included 405 patients and identified an optimal cMRD cutoff at 0.56% of WBCs. By applying this cutoff, 10.4% (42/405) of patients were classified as cMRD+, compared to 14.8% (60/405) using the recommended 0.1% cutoff for mgMRD. cMRD and mgMRD status were concordant in 85.2% (345/405) of patients. In the mgMRD-/cMRD+ group (n=21), the 5-year CIR was 54.0%, whereas in the mgMRD+/cMRD- group (n=39) it was 31.5%, comparable to the mgMRD-/cMRD- group (37.1%, n=324).

The 5-year OS, RFS, and CIR was similar for the MRD negative groups regardless of method (Figure 1). The 5-year RFS of cMRD+ patients was 25.3% (CI: 14.7%−43.6%) while it was 41% for mgMRD+ patients (CI: 30.0% - 56.2%). For CIR, a significant survival difference for cMRD (sHR: 2.07; $p<0.01$) was found, whereas this effect was absent for mgMRD (sHR: 1.24; $p=0.32$).

Conclusion: Computational MRD assessment using our newly developed pipeline delivers a fast and objective MRD assessment with clinically relevant survival associations compared to manual gating. Ongoing expert re-evaluation of discrepant cases may reveal whether computational analysis can enhance the characterization of leukemia-associated immunophenotypes associated with relapse.

Keywords: acute myeloid leukemia, measurable residual disease, flow cytometry, machine learning

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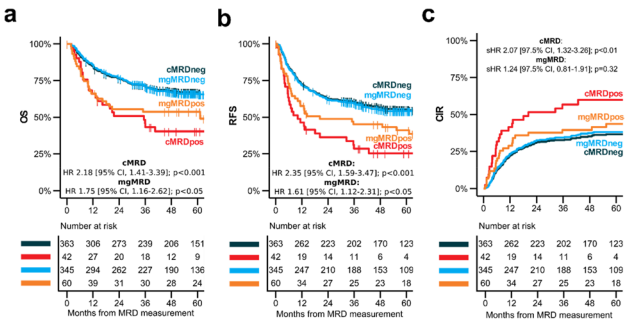
Fig P052-1 A, B, C. Prognostic value of computational MRD assessment (cMRD) in AML. (A) Kaplan-Meier curve for OS. (B). Kaplan-Meier curve for RFS. (C) Kaplan-Meier curve for CIR. Hazard ratios were calculated by Cox proportional hazards (OS, RFS) or by proportional subdistribution hazards (CIR)



P053. Primitive marker-based measurable residual disease in acute myeloid leukemia in the context of hemodilution

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Background: Measurable residual disease (MRD) detected by multiparameter flow cytometry (MFC) is a validated biomarker for relapse prediction in acute myeloid leukemia (AML) after two cycles of chemotherapy. MRD is traditionally defined as the proportion of leukemia-associated immunophenotype (LAIP) positive cells within the white blood cell (WBC) compartment. Hemodilution during bone marrow aspiration may therefore lead to false negative MRD results when using this WBC-MRD approach. Primitive marker MRD (PM-MRD), defined as the proportion of LAIP-positive cells within the primitive cell compartment (CD34+, CD117+, or CD133+ cells), is, theoretically, less sensitive to hemodilution. This study aimed to validate the prognostic value of PM-MRD in a large cohort and investigate its relevance in the context of hemodilution.

Methods: We included patients in complete morphologic remission after two cycles of intensive chemotherapy from six HOVON trials (H42A, H81, H92, H102, H103, H132). Patients with PM-MRD ≥ 10% were considered positive, provided the primitive cell count exceeded our assay's background level (0.03% of total WBC). To assess the prevalence of hemodilution, we examined 250 randomly selected samples from the H132 trial measured at Amsterdam UMC. Hemodilution was defined based on mast cell percentage (CD117 bright) below 0.002% (1) of ≥ 500,000 WBC.

Results: Of the 857 patients, 152 (18%) were PM-MRD positive. PM-MRD ≥10% was associated with significantly worse overall survival (HR: 1.44, 1.12–1.84 [Figure 1A]) and relapse-free survival (HR: 1.32, 1.05 −1.66) compared to PM-MRD <10%. However, a combined model of WBC-MRD and PM-MRD demonstrated that WBC-MRD appears to have stronger prognostic value [Figure 1B]. Mast cell-based analysis revealed that 52% of the 234 valid samples were hemodiluted [Figure 1C]. Hemodiluted samples had a significantly lower median WBC-MRD percentage than non-hemodiluted samples, while PM-MRD remained stable across both groups [Figure 1D].

Conclusion: This study aimed to validate PM-MRD as a prognostic biomarker in AML. However, PM-MRD did not seem to improve risk stratification compared to conventional WBC-MRD. The finding that 52% of cases were hemodiluted, suggests that the prevalence of hemodilution might generally be underestimated, while its ultimate impact on the prognostic relevance of standard WBC-MRD might be limited. Our data must be confirmed by other centers and warrant further research on the effect of hemodilution on the prognostic value of MRD.

Keywords: acute myeloid leukemia, measurable residual disease, flow cytometry, hemodilution

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