Upfront Allogeneic Stem Cell Transplantation with Individualized Venetoclax-Based Conditioning in *MECOM*-Rearranged Acute Myeloid Leukemia – a Single-Center Retrospective Study

M. Mikalonytė[1,2], M. Tamutytė-Jankauskė[1,2], T. Smalinskaitė[1,2], G. Daukėlaitė[1,2], L. Kevličius[1], L. Davainis[1], I. Trociukas[1], A. Slobinas[1], R. Jucaitienė[1], I. Šlepikienė[1], R. Kviliūtė[1], R. Batiuškaitė[1], L. Griškevičius[1,2], A. Žučenka[1]

1 Vilnius University Hospital Santaros Klinikos, Hematology, Oncology, and Transfusion Medicine Center, Vilnius, Lithuania

2 Vilnius University, Faculty of Medicine, Institute of Clinical Medicine, Vilnius, Lithuania

Vilnius University Hospital SANTAROS KLINIKOS

Faculty of Medicine

INTRODUCTION

MECOM-rearranged (*MECOMr*) AML is highly chemorefractory, with CR rates around 30% following conventional induction. Allogeneic HSCT remains the only curative option.[1-3] We report a strategy in which *MECOMr* AML patients proceed directly to allo-HSCT with individualized venetoclax-based conditioning without achieving pre-transplant CR.

AIM

To evaluate the efficacy and toxicity of direct-to-transplant strategy in *MECOMr* AML patients.

METHOD

A single-center retrospective study (2023–2026) with 15 adult *MECOMr* AML patients, who proceeded directly to allo-HSCT without achieving pre-transplant CR. Patients received individualized venetoclax-based sequential conditioning — De-FLAG-Ida-Ven, DC-ACTIVE, or ARCHIVE-based regimens with alkylator-based myeloablation. Main outcome measures: MLFS at allo-HSCT; best posttransplant response; MRD negativity (flow <0.1%); OS; relapse; day-30/60 mortality; grade 3–4 acute GVHD; grade ≥3 infections; and engraftment kinetics.

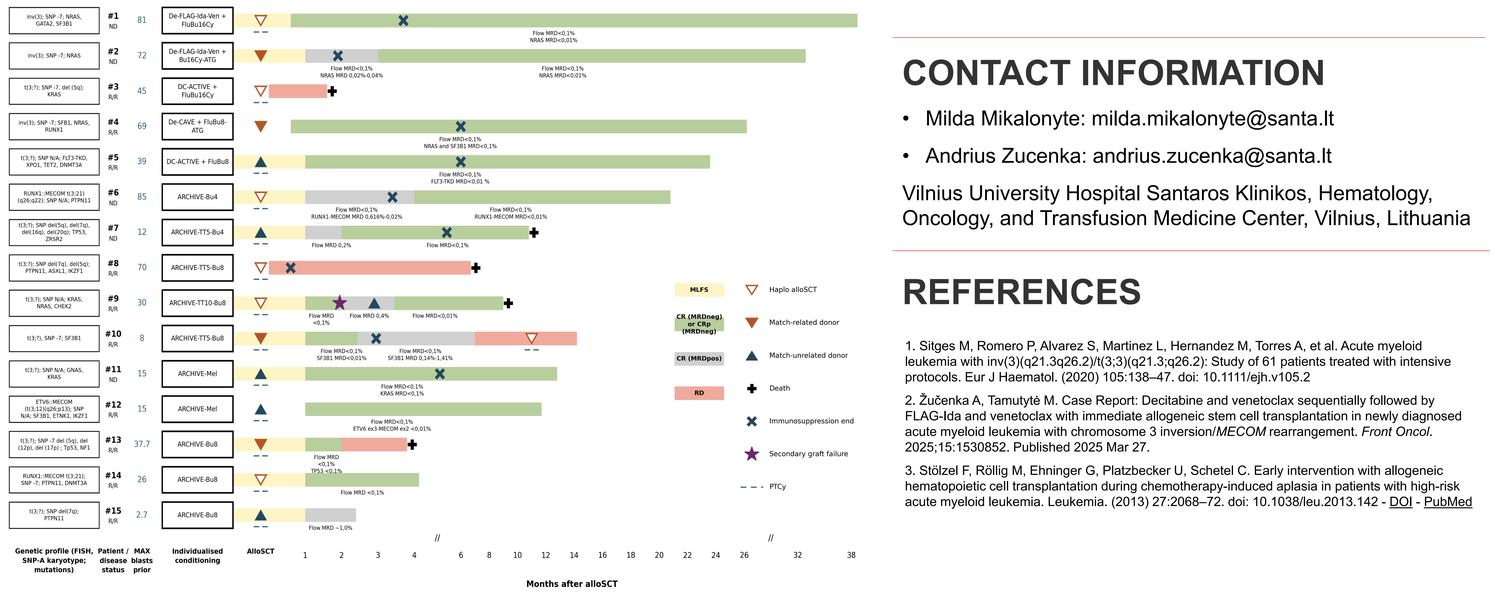
CONCLUSIONS

Upfront allo-HSCT with individualized venetoclax-based conditioning, without requiring pre-transplant CR, is feasible in *MECOMr* AML and yields high post-transplant CR/CRp and MRD negativity rates with low early mortality. Relapses and infectious complications remain the main drivers of mortality. Findings warrant cautious interpretation given the small retrospective cohort.

RESULTS

Baseline Characteristic & Demographics	N = 15
Age, median (range)	**56 (23–69)**
Female sex, % (n/N)	**64.3 (10/15)**
Median ECOG performance status, (range)	**1 (0-2)**
Complex karyotype, % (n/N)	**35.7 (6/15)**
Co-occurring with Monosomy 7, % (n/N)	**50.0 (8/15)**
Pre-Transplant Status & Donors	
Max pre-conditioning blast count, median (range)	**34.5% (2.7–85%)**
CR at transplant, % (n/N)	**0 (0/15)**
MLFS at transplant, % (n/N)	**80.0 (12/15)**
Haploidentical donor, n	**6**
Matched unrelated donor, n	**6**
Matched related donor, n	**3**

Efficacy & Post-Transplant Outcomes	N = 15
Best Response: CR, % (n/N)	**80.0 (12/15)**
Best Response: CRp, % (n/N)	**6.7 (1/15)**
MRD negativity, % (n/N)	**80.0 (12/15)**
Median time to neutrophil engraftment	**20.5 days**
Median time to platelet engraftment	**28.0 days**
Newly diagnosed subgroup (n=5) CR & MRD negative	**100% (6/6)**
Safety, Complications & Follow-up	
Grade 3–4 acute GVHD, % (n/N)	**13.3 (2/15)**
Grade ≥3 infections, % (n/N)	**85.7 (13/15)**
Day-30 / Day-60 mortality, n	**0 / 1**
Median OS / Ongoing CR / Relapsed, n	**NR / 9 / 3**
Total Deaths (including TRM)	**5 (2 TRM)**



CONTACT INFORMATION

- Milda Mikalonyte: milda.mikalonyte@santa.lt
- Andrius Zucenka: andrius.zucenka@santa.lt

Vilnius University Hospital Santaros Klinikos, Hematology, Oncology, and Transfusion Medicine Center, Vilnius, Lithuania

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Abbreviations: allo - allogeneic; AML - acute myeloid leukemia; ARCHIVE - alkylating agents, cytarabine, hypomethylating agent(s), cladribine, and venetoclax; CR - complete response; CRp - complete response with incomplete platelet recovery; DC-ACTIVE - decitabine, cladribine, venetoclax, low-dose cytarabine, actinomycin D; De-FLAG-IDA-Ven - decitabine, fludarabine, granulocyte colony-stimulating factor, cytarabine, idarubicin, and venetoclax; ELN - European Leukemia Network; GVHD - graft-versus-host disease; HSCT - hematopoietic stem cell transplantation; *MECOM* - MDS1 and EVI1 complex locus; MLFS - morphologic leukemia-free state; MRD - measurable residual disease; OS - overall survival; PTCy – post-transplant cyclophosphamide; TRM – treatment related mortality