SUSTAINED REMISSION OF NPM1/IDH1-MUTATED ACUTE MYELOID LEUKEMIA FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT IN A PATIENT WITH END-STAGE HEART FAILURE REQUIRING LVAD SUPPORT

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Introduction

- **AML with severe cardiomyopathy represents a major therapeutic challenge**, as HSCT is often deemed prohibitive when LVEF <20%. Current HSCT guidelines typically exclude patients with LVEF ≤35%, though risk vs benefit discussion in certain cases should be considered, especially with the collaborative effort of a multidisciplinary team[1].
- **Evidence on HSCT outcomes in patients with profound cardiac dysfunction is extremely limited**, especially in those supported with durable LVADs.
- **We report a rare case of NPM1/IDH1-mutated AML** achieving long-term, MRD-negative remission after HSCT despite end-stage heart failure requiring LVAD support.

Discussion

- **HSCT is not commonly performed in patients with severe cardiac dysfunction**
  Patients with AML and advanced cardiomyopathy are often excluded from transplant due to the high risk of peri-transplant morbidity and mortality. This case illustrates that HSCT can be successfully pursued when optimal supportive care and cardiac interventions are in place.
- **Literature remains sparse.**
  Few reports describe HSCT in patients with LVEF <35%, and most involve milder dysfunction[2,3]. Pediatric and adult cases with LVEF between 25–38% have been transplanted successfully[4], but our patient represents one of the first documented cases with **LVEF <20% requiring LVAD support.**

This case illustrates that HSCT can be feasible in AML with severe cardiac dysfunction. Despite advanced heart failure requiring LVAD, the patient achieved long-term MRD-negative remission through close survivorship care and multidisciplinary collaboration.

Case Presentation

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- **Patient:** 50-year-old male with history of viral myocarditis/cardiomyopathy (LVEF 20–25%)
- **AML Diagnosis (2017):** NPM1/IDH1-mutated AML; normal karyotype; marrow with 70% blasts. Anthracycline was deferred due to cardiac dysfunction.

Treatment Course:

- **Induction/Consolidation:** FLAG induction → 4 cycles HiDAC → CR1 (7 months).
- **Relapse 1:** Salvage FLAG → CR2 (6 months, HSCT deferred for cardiac comorbidity).
- **Relapse 2:** Salvage azacitidine/venetoclax → CR3 (MRD-positive by NPM1 PCR).

Transplant:

- Underwent **reduced-intensity conditioning HSCT** (Busulfan/Fludarabine; 10/10 PBSC MUD GVHD ppx: ATG/Tacrolimus/methotrexate in MRD-positive CR3.
- **Complications:** Prolonged ICU stay for multifocal pneumonia, recurrent septic/cardiogenic shock, and ventricular tachycardia storm.
- **Long-Term Outcome:** Developed chronic GVHD (eyes, mouth, lung). In 2022, LVAD was placed for refractory ventricular arrhythmias and recurrent decompensated heart failure.

Current Status:

- Five years post-HSCT: sustained MRD-negative remission by NPM1 PCR.
- Clinically stable with LVAD support, no AML relapse, and no further hospitalizations for acute decompensated heart failure.

Discussion

Key factors supporting a favorable outcome included:

- **Anthracycline-sparing induction (FLAG)** to avoid cardiotoxicity.
- **Effective salvage with azacitidine/venetoclax**, enabling CR3 (despite MRD+ status).
- **Reduced-intensity conditioning (Bu/Flu)** to limit toxicity, and avoidance of PTCy for GVHD ppx
- **Durable circulatory support with LVAD**, preventing recurrent decompensated heart failure
- **Multidisciplinary management is critical.**
  Integration of hematology/oncology, transplant medicine, and cardiology was essential for risk stratification, peri-transplant management, and long-term survivorship. This highlights the need for **collaborative decision-making** in dual-organ dysfunction
- **Implications for practice.**
  While reduced LVEF is a relative contraindication, this case suggests it should not be viewed as an **absolute barrier to HSCT**. With modern heart failure therapies—including LVAD support—select patients can achieve durable leukemia control.
- **Future directions.**
  Additional studies are needed to define **selection criteria, conditioning regimens, and peri-transplant cardiac optimization strategies** for this high-risk group. Until then, individual case experiences like this contribute important evidence to guide practice.

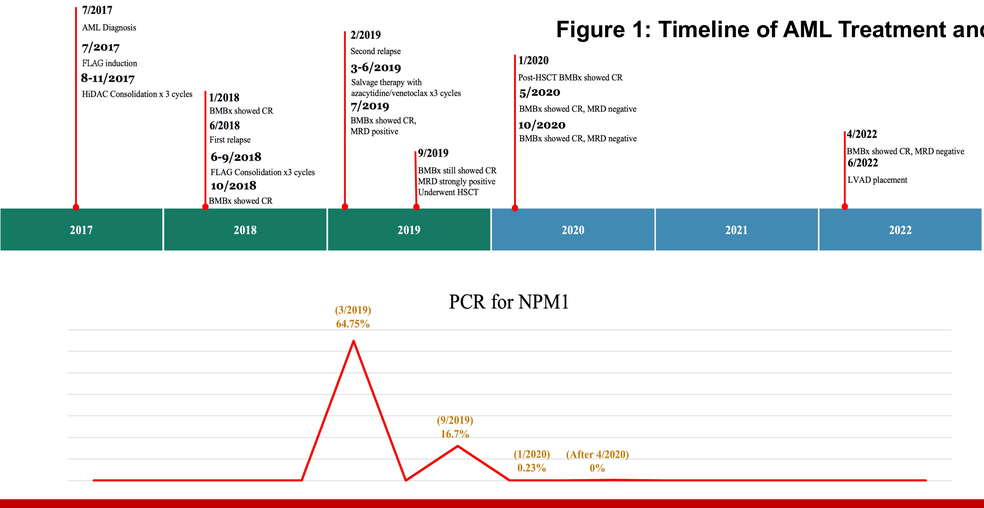


Figure 1: Timeline of AML Treatment and NPM1 PCR Response

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