MYELOVAC: A Phase I Trial of a Personalized Neoantigen Peptide Vaccination Platform in Combination with Hypomethylating Agent-Based Therapy for Patients with Acute Myeloid Leukemia in First Complete Remission Ineligible for Intensive Chemotherapy and Allogeneic Stem Cell Transplantation

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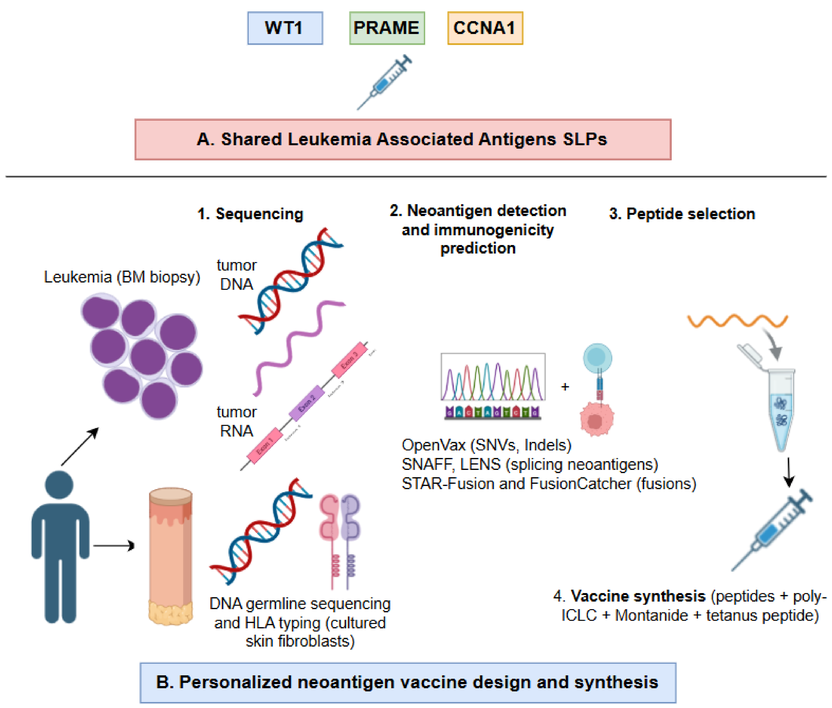
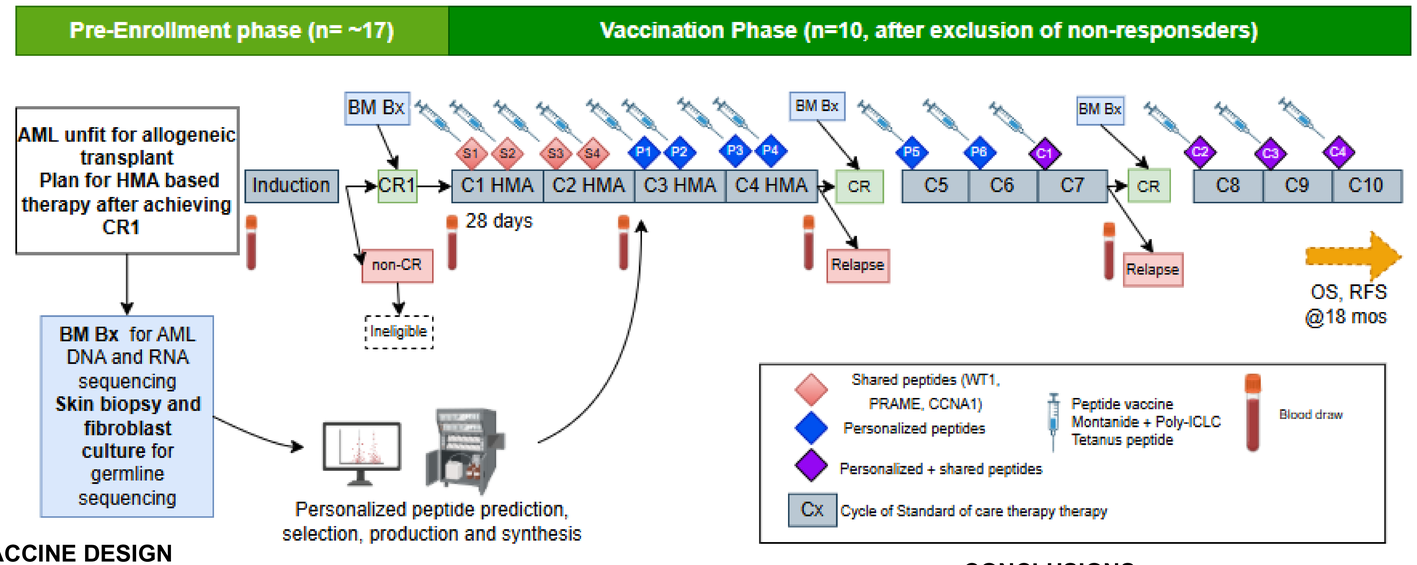
INTRODUCTION

- AML patients unfit for intensive chemotherapy and allo-HCT receiving hypomethylating agent (HMA)-based therapy achieve ~60% initial response, but ~70% relapse with high mortality
- Low tumor mutation burden (TMB), shared antigen expression between leukemic and healthy cells, and immunosuppressive milieu have impeded immunotherapy efforts
- Personalized neoantigen vaccination with mRNA and peptide vaccines has recently been shown to be immunogenic and potentially improve patient outcomes in solid tumors [1-3]
- Alternative neoantigen resources such as splicing and fusion neoantigens could be utilized to overcome low TMB
- Several driver mutations of AML (NPM1, FLT3, IDH2) have been shown to be immunogenic
- HMAs have been shown to upregulate several leukemia associated antigens [4]
- Personalized peptide-based neoantigen vaccination could offer a promising strategy to induce antitumor immunity and it has not been tested in AML

AIM

To determine the safety, tolerability, and feasibility of MYELOVAC, a peptide-based vaccine platform combining shared leukemia-associated antigens (LAAs) with patient-specific neoantigens, in AML patients in first complete remission (CR1) with HMA-based therapy





VACCINE DESIGN

Integrates four antigen sources:

- Shared LAAs targeting WT1 [5], PRAME [6], and Cyclin A1 [7]
- Personalized neoantigens from somatic mutations, splicing events, and gene fusions
- Adapts the PGV001 platform (safe and immunogenic in solid cancers and myeloma). Administered with poly-ICLC and Montanide adjuvants concurrently with HMA-based therapy.

STUDY DESIGN

- Single-center phase I pilot trial
- Pre-enroll at diagnosis: tissue banking (BM aspirate + skin biopsy) + neoantigen ID
- Vaccination begins at confirmed CR1
- DLTs assessed across two 28-day windows
- Schedule: 4 shared doses/2mo → 6 personalized doses/4mo → 4 combined monthly doses

Patients

- Adults ≥18 years with AML, unfit for intensive chemo and HCT
- Achieving CR/CRi; planned HMA-based therapy; can be MRD positive
- ECOG 0-3; active autoimmune disease past 1 yr excluded
- Target enrollment: N=10

Endpoints

- Primary: DLT rate (safe if ≤2/10 DLTs)
- Secondary: feasibility, immunogenicity (IFN-γ ELISPOT, ICS staining), MRD conversion (flow/PCR), RFS and OS at 18 months
- Exploratory: Bone marrow microenvironment changes before and after vaccination (scRNA seq, TCR seq, comparison of ongoing remission samples and relapse samples with baseline)

CONCLUSIONS

- MYELOVAC is the first personalized neoantigen peptide vaccine effort for AML
- Targets multiple antigen classes combined with HMA-based therapy, which may enhance immune priming and improve vaccine response
- Aims to inform vaccination efforts in AML; enrollment anticipated early 2027

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