NCI National Clinical Trials Network

MM1OA-EA02

ECOG-ACRIN cancer research group

Please Enroll Your Eligible Patients!

For Patients with Acute Myeloid Leukemia

MM1OA-EA02 Available Through ECOG-ACRIN Cancer Research Group

A Randomized Phase II Study of Venetoclax and HMA-based Therapies for the Treatment of Older and Unfit Adults with Newly Diagnosed FLT3-mutated Acute Myeloid Leukemia: A MyeloMATCH Treatment Trial

Patient Population

See Section 3 for complete eligibility criteria

- Age ≥ 60, or < 60 who in the opinion of the treating physician are better served by azanucleoside-based therapy rather than intensive, cytarabine-based induction based on clinical status (i.e., performance status, age > 75 years), organ dysfunction, or disease biology
- Must have a morphologically confirmed diagnosis of AML according to the WHO 2016 classification excluding APL with PML-RARA, AML with RUNX1-RUNX1T1, or AML with CBFB-MYH11
- Must have no prior therapy for AML with the exception of hydroxyurea and all-trans retinoic acid (ATRA), or leukapheresis
  - ◊ Patients with cytarabine-based emergency therapy prior to the start of therapy on this trial are eligible
- Must have no prior therapy with hypomethylating agents or FLT3 inhibitors
- Must have the FLT3-ITD or D835 mutation based on the MyeloMATCH Master Screening and Reassessment Protocol (MSRP); must be assigned to MM1OA-EA02 by the MyeloMATCH MSRP
- Adequate lab values per protocol
- HIV, HBV, or HCV-infected patients are eligible per protocol
- Must not have a baseline corrected QT interval ≥ 480 msec using Fredericia correction (QTcF)
- Must not have the medical necessity for ongoing treatment with a strong CYP3A4 inducing drug
- Patients with prior/current malignancy whose natural history or treatment does not have the potential to interfere with the safety/efficacy assessment of the investigational regimen are eligible
- Patients with known history/current symptoms of cardiac disease, or history of treatment with cardiotoxic agents should be NYHA class 2B or better
- Must not have an active or uncontrolled infection

Treatment Plan

See Section 5 for complete treatment details

Cycle = 28 days

Regimen 1: Azacitidine + Venetoclax

- **Induction Cycle 1:** Azacitidine 75 mg/m² IV or SQ on Days 1-7; Venetoclax 100 mg PO on Day 1, 200 mg on Day 2, 400 mg on Days 3-28
- **Induction Cycle 2:** Azacitidine 75 mg/m² IV or SQ on Days 1-7; Venetoclax 400 mg PO on Days 1-28
- **Consolidation:** Azacitidine 75 mg/m² IV or SQ on Days 1-7; Venetoclax 400 mg PO on Days 1-28

Regimen 2: Azacitidine + Venetoclax + Gilteritinib

- **Induction Cycle 1:** Azacitidine 75 mg/m² IV or SQ on Days 1-7; Venetoclax 100 mg PO on Day 1, 200 mg on Day 2, 400 mg on Days 3-28; Gilteritinib 80 mg PO on Days 1-28
- **Induction Cycle 2:** Azacitidine 75 mg/m² IV or SQ on Days 1-7; Venetoclax 400 mg PO on Days 1-28; Gilteritinib 80 mg PO on Days 1-28
- **Consolidation:** Azacitidine 75 mg/m² IV or SQ on Days 1-5; Venetoclax 400 mg PO on Days 1-7; Gilteritinib 80 mg PO on Days 1-28

Regimen 3: Azacitidine + Venetoclax + Gilteritinib

- **Induction Cycle 1:** Azacitidine 75 mg/m² IV or SQ on Days 1-7; Venetoclax 100 mg PO on Day 1, 200 mg on Day 2, 400 mg on Days 3-28; Gilteritinib 80 mg PO on Days 8-21
- **Induction Cycle 2:** Azacitidine 75 mg/m² IV or SQ on Days 1-7; Venetoclax 400 mg PO on Days 1-28; Gilteritinib 80 mg PO on Days 8-21
- **Consolidation:** Azacitidine 75 mg/m² IV or SQ on Days 1-5; Venetoclax 400 mg PO on Days 1-14; Gilteritinib 80 mg PO on Days 8-21

Regimen assignments are randomized; crossover not permitted. Induction therapy is 2 cycles or until remission, whichever comes first. Consolidation therapy may given up to 2 years. Conditions per Section 5.1 must be met before consolidation.

Study Chair:
Jessica K. Altman, MD

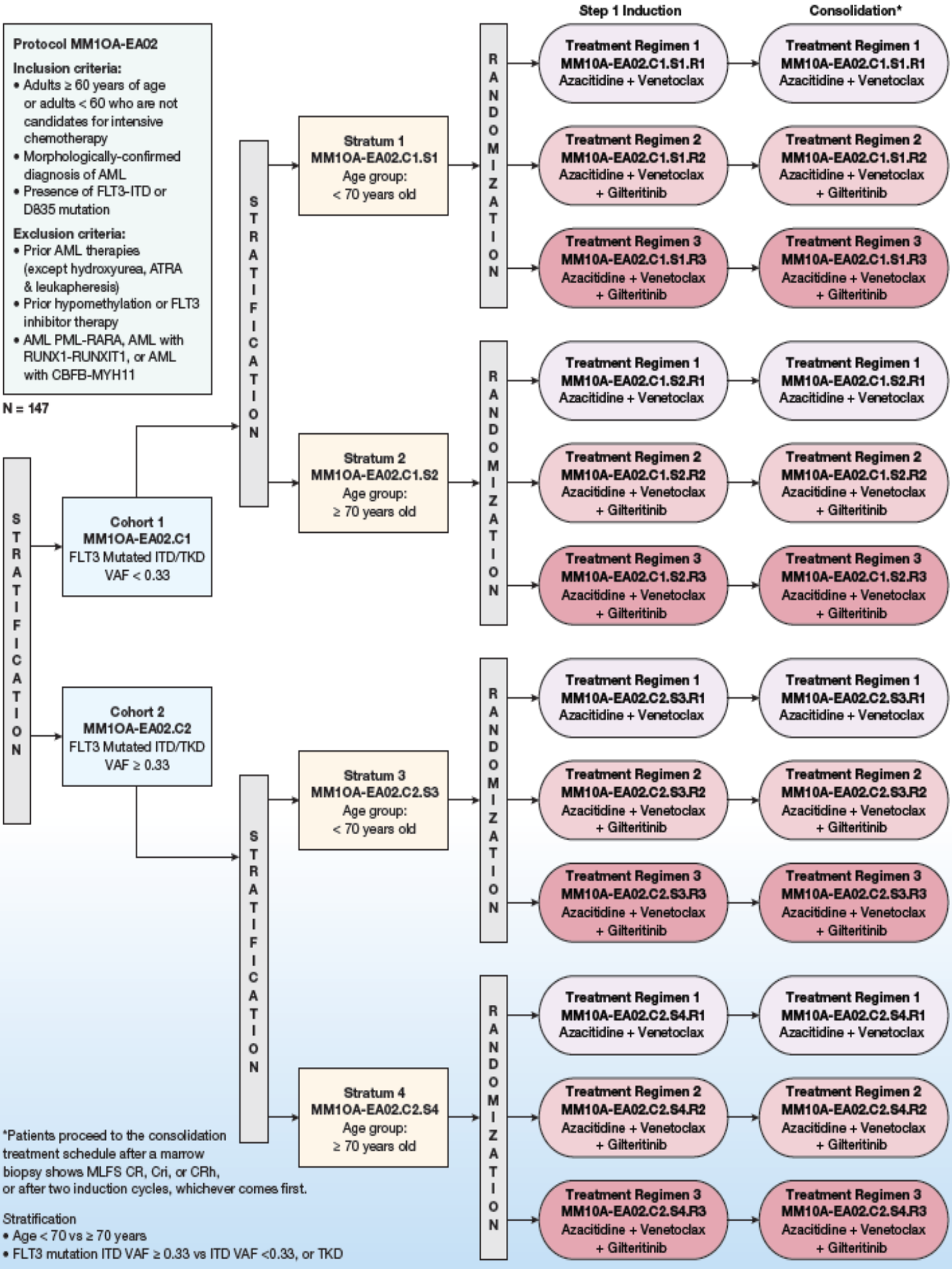
Study Co-Chair:
Alexander E. Perl, MD

Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

https://open.ctsu.org/open 1-888-823-5923

Protocol Information (ECOG-ACRIN Operations – Boston)

http://ecog-acrin.org (Member Login) 1-857-504-2900


Step 1 Induction
Consolidation*
Protocol MM1OA-EA02
Inclusion criteria:
• Adults ≥ 60 years of age or adults < 60 who are not candidates for intensive chemotherapy
• Morphologically-confirmed diagnosis of AML
• Presence of FLT3-ITD or D835 mutation
Exclusion criteria:
• Prior AML therapies (except hydroxyurea, ATRA & leukapheresis)
• Prior hypomethylation or FLT3 inhibitor therapy
• AML PML-RARA, AML with RUNX1-RUNXIT1, or AML with CBFB-MYH11
N = 147
STRATIFICATION
Cohort 1
MM1OA-EA02.C1
FLT3 Mutated ITD/TKD
VAF < 0.33
Cohort 2
MM1OA-EA02.C2
FLT3 Mutated ITD/TKD
VAF ≥ 0.33
STRATIFICATION
Stratum 1
MM1OA-EA02.C1.S1
Age group:
< 70 years old
Stratum 2
MM1OA-EA02.C1.S2
Age group:
≥ 70 years old
Stratum 3
MM1OA-EA02.C2.S3
Age group:
< 70 years old
Stratum 4
MM1OA-EA02.C2.S4
Age group:
≥ 70 years old
RANDOMIZATION
Treatment Regimen 1
MM10A-EA02.C1.S1.R1
Azacitidine + Venetoclax
Treatment Regimen 2
MM10A-EA02.C1.S1.R2
Azacitidine + Venetoclax + Gilteritinib
Treatment Regimen 3
MM10A-EA02.C1.S1.R3
Azacitidine + Venetoclax + Gilteritinib
Treatment Regimen 1
MM10A-EA02.C1.S2.R1
Azacitidine + Venetoclax
Treatment Regimen 2
MM10A-EA02.C1.S2.R2
Azacitidine + Venetoclax + Gilteritinib
Treatment Regimen 3
MM10A-EA02.C1.S2.R3
Azacitidine + Venetoclax + Gilteritinib
Treatment Regimen 1
MM10A-EA02.C2.S3.R1
Azacitidine + Venetoclax
Treatment Regimen 2
MM10A-EA02.C2.S3.R2
Azacitidine + Venetoclax + Gilteritinib
Treatment Regimen 3
MM10A-EA02.C2.S3.R3
Azacitidine + Venetoclax + Gilteritinib
Treatment Regimen 1
MM10A-EA02.C2.S4.R1
Azacitidine + Venetoclax
Treatment Regimen 2
MM10A-EA02.C2.S4.R2
Azacitidine + Venetoclax + Gilteritinib
Treatment Regimen 3
MM10A-EA02.C2.S4.R3
Azacitidine + Venetoclax + Gilteritinib
*Patients proceed to the consolidation treatment schedule after a marrow biopsy shows MLFS CR, Cri, or CRh, or after two induction cycles, whichever comes first.
Stratification
• Age < 70 vs ≥ 70 years
• FLT3 mutation ITD VAF ≥ 0.33 vs ITD VAF <0.33, or TKD