NCI National Clinical Trials Network

EA4151

ECOG-ACRIN cancer research group

For Patients with Mantle Cell Lymphoma

EA4151 Available Through ECOG-ACRIN Cancer Research Group

A Randomized Phase III Trial of Consolidation with Autologous Hematopoietic Cell Transplantation Followed by Maintenance Rituximab vs. Maintenance Rituximab Alone for Patients with Mantle Cell Lymphoma in Minimal Residual Disease-Negative First Complete Remission

Patient Population

See Section 3.0 for Complete Eligibility Details

Eligibility for Screening (Step 0– Pre-registration):

- Age ≥ 18 and ≤ 70 years
- Must have histologically confirmed mantle cell lymphoma, with cyclin D1 by immunohistochemical stains and/or t (11;14) by cytogenetics/FISH (see protocol for details)
- Enrolling physician must feel that the patient is a candidate for autologous stem cell transplantation
- May be about to begin/be receiving/have completed induction therapy within 120 days prior to pre-registration to Step 0. No more than 300 days may have passed between the first day of induction therapy and pre-registration
  - ◊ For patients that completed induction therapy, re-staging evaluation must show PR/CR; post-induction patients with clinical disease progression are not eligible for pre-registration
  - ◊ Up to 2 regimens of chemotherapy are allowed as long as continuous response was ongoing throughout therapy (a PR must be achieved)
- No documented history of CNS involvement by mantle cell lymphoma

Eligibility for Treatment Assignment (Step 1):

- Proliferation rate, using Ki-67/MIB-1 must be documented
- Must have received results from FFPE submission: MRD Indeterminate, or identified unique clonal immunoglobulin DNA sequence and MRD assessment completed
- Must have completed induction therapy within 150 days prior to registration to Step 1 AND no more than 300 days elapsed from the first dose of induction chemo given, until the last day of induction chemo administered
  - ◊ Must have received at least 4 cycles; up to 2 regimens allowed as long as continuous response was ongoing
- ECOG PS 0-2; must have radiologic complete/partial remission (Lugano)
- HIV positive patients must meet criteria per protocol

Treatment Plan

See Section 5.0 for Complete Treatment Details

Patient treatment assignment is as follows:

- Arm A or B: clonal molecular marker identified, blood MRD negative, ≥ 100,000 total nucleated cells analyzed for MRD, complete response (Lugano)
- Arm C: clonal molecular marker identified, blood MRD positive, complete/partial response
- Arm D: clonal molecular marker identified, blood MRD indeterminate, complete/partial response; OR no clonal molecular marker identified; OR clonal molecular marker, blood MRD negative, partial response; OR clonal molecular marker, blood MRD negative, < 100,000 nucleated cells for MRD

Arm A: HCT; Rituximab maintenance 375 mg/m² IV or Rituxan Hycela 1400 mg/23,400 units SQ (or approved rituximab biosimilar) every 8 wks (+/- 1 wk) x 18 doses (to begin 100-140 days after transplant). **Arm B:** Rituximab maintenance 375 mg/m² IV or Rituxan Hycela 1400 mg/23,400 units SQ (or approved rituximab biosimilar), every 8 wks (+/- 1 wk) x 18 doses (to begin 40-180 days after completion of induction therapy). **Arm C:** HCT (Note: blood must be submitted at Day 100 [+/- 5 days] post-transplant for MRD assessment); Rituximab maintenance 375 mg/m² IV or Rituxan Hycela 1400 mg/23,400 units SQ (or approved rituximab biosimilar) every 8 wks (+/- 1 wk) x 18 doses (to begin 100-140 days after transplant). **Arm D:** HCT; Rituximab maintenance 375 mg/m² IV or Rituxan Hycela 1400 mg/23,400 units SQ (or approved rituximab biosimilar) every 8 wks (+/- 1 wk) x 18 doses (to begin 100-140 days after transplant)

Notes (see protocol for details):

- *Remission induction therapy is not considered protocol therapy, but it may impact the patient's eligibility to register to treatment*
- *HCT will be performed per institutional guidelines; rituximab administration to be managed per standard of care; up to 4 doses of maintenance rituximab may be held due to COVID-19 infection/to facilitate vaccination*

Study Chair: Timothy S. Fenske, MD, MS

SWOG Co-Chair: Brian Till, MD

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BMT CTN Chair: Matt Lunning, MD

BMT Co-Chair: Hillard Lazarus, MD

Patient Enrollment

All Sites: Oncology Patient Enrollment Network (OPEN) https://open.ctsu.org

Protocol Information

ECOG-ACRIN Operations-Boston: 857-504-2900, http://ecog-acrin.org (Member Login)

Please Enroll Your Eligible Patients!

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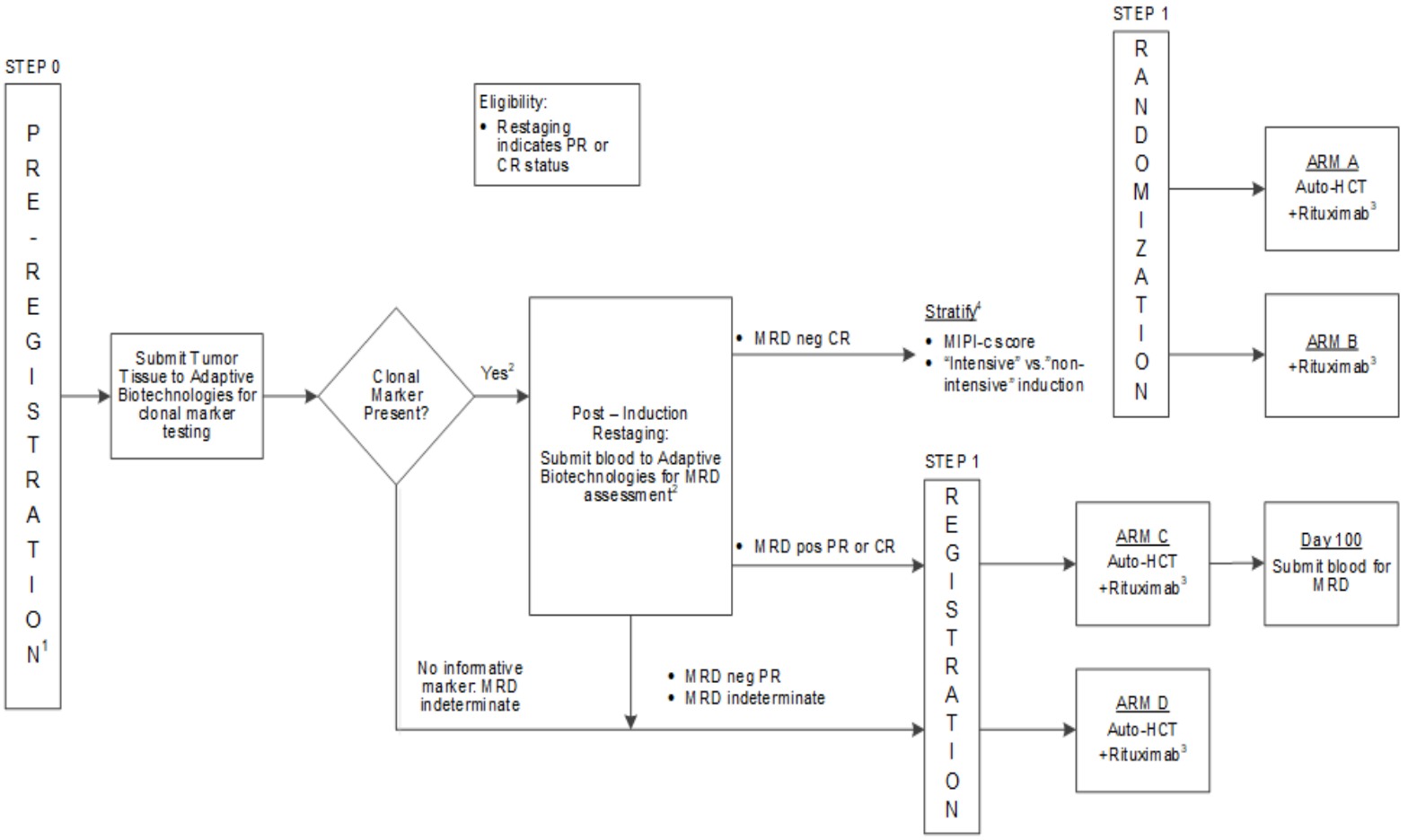
EA4151



N = 689 patients

1. Patients may be pre-registered to STEP 0 either just prior to starting induction, during induction or within 120 days following completion of induction. Patients need to at least have a PR to get assigned to an arm. If they have SD or PD to induction, they are not eligible for arm assignment. Patients who are pre-registered after completion of induction must have achieved a PR or CR status.
2. Sites will be notified of the results of the clonal assessment. Patients for whom a marker exists and at restaging are found to have complete or partial response (CR or PR), blood must be submitted for determination of minimal residual disease (MRD) status. Blood must be collected at time of or after restaging and should not be submitted until after notification of clonal marker status. If blood was submitted at the same time the tumor tissue was submitted for clonal marker evaluation, only blood from patients with a clonal marker signature will be evaluated.
3. Rituximab maintenance: rituximab 375 mg/m2 IV or Rituxan Hycela 1400 mg/23,400 Units SQ q8 weeks x 3 years.
4. Patients need to at least have a PR to get assigned to an arm. If they have SD or PD to induction, they are not eligible for arm assignment.