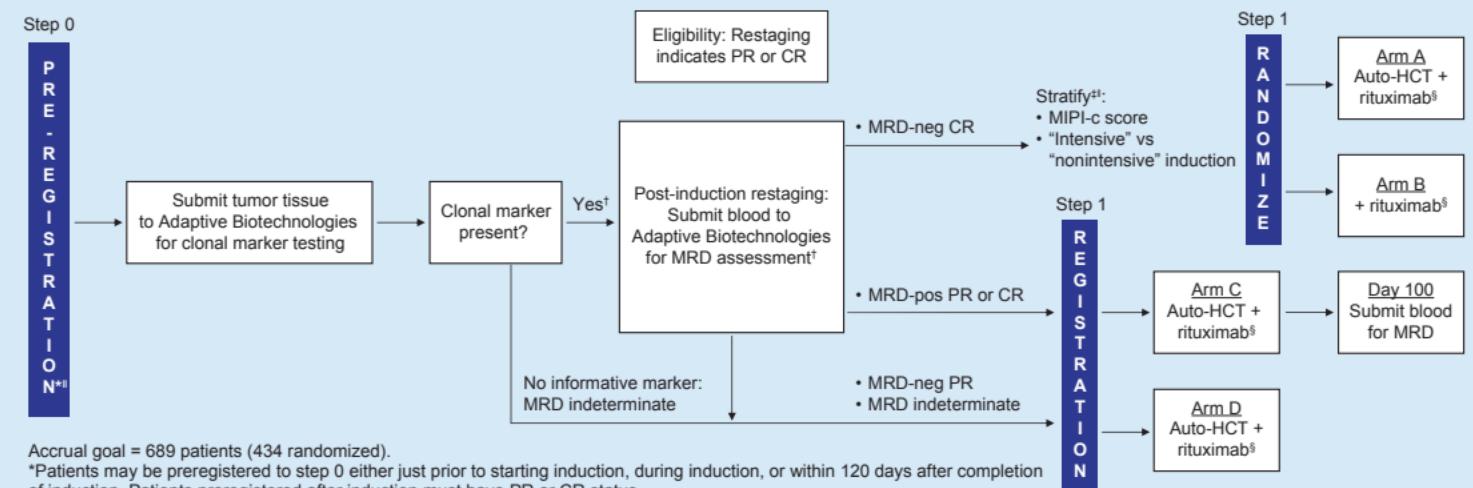




A Randomized Phase III Trial of Consolidation With Autologous Hematopoietic Cell Transplantation Followed by Maintenance Rituximab vs. Maintenance Rituximab Alone for Patients With Mantle Cell Lymphoma in Minimal Residual Disease-Negative First Complete Remission

Study Schema



Accrual goal = 689 patients (434 randomized).

*Patients may be preregistered to step 0 either just prior to starting induction, during induction, or within 120 days after completion of induction. Patients preregistered after induction must have PR or CR status.

†Sites will be notified of clonal assessment results. In patients for whom a marker exists and who have CR or PR at restaging, blood is submitted to determine MRD status. Blood is collected at, or after, restaging and not submitted until after notification of clonal marker status. If blood was submitted when the tumor was submitted for clonal marker evaluation, only blood from patients with a clonal marker signature is evaluated.

‡Patients are stratified by induction regimen and MIPI-c score (calculated using data from the time of diagnosis). The induction regimen has 2 categories: containing high-dose cytarabine vs lacking high-dose cytarabine. For MIPI-c score there will be 4 categories: low, low/intermediate, high/intermediate + high, and "not determined."

§Rituximab maintenance: rituximab 375 mg/m² IV or Rituxan Hycela 1400 mg/23,400 units SC q 8 weeks × 3 years. NOTE: 18 total doses of rituximab maintenance should be given, but up to 4 doses may be held due to COVID-19 infection/facilitation of vaccination.

†Patients need to at least have a PR to get assigned to an arm.

auto-HCT= autologous hematopoietic cell transplantation; CR = complete response; MIPI-c = Mantle Cell Lymphoma International Prognostic Index combined; MRD = minimal residual disease; PR = partial response.

EA4151

Overall EA4151 Study Objective

To examine whether autologous hematopoietic cell transplantation (auto-HCT) followed by maintenance rituximab, compared with maintenance rituximab alone, can provide a survival benefit in mantle cell lymphoma (MCL) patients that have achieved a minimal residual disease (MRD)-negative complete remission (CR) following induction therapy.

Study Objectives

Primary Objective

- Compare overall survival (OS) in MCL patients in MRD-negative first CR who undergo auto-HCT followed by maintenance rituximab versus maintenance rituximab alone (without auto-HCT)

Secondary Objectives

- Compare progression-free survival (PFS) in MCL patients with MRD-negative CR who undergo auto-HCT followed by maintenance rituximab versus maintenance rituximab alone
- Define OS and PFS at 2 and 5 years of chemosensitive but MRD-positive CR and partial remission (PR) patients who undergo auto-HCT followed by 3 years of maintenance rituximab

- Define OS and PFS at 2 and 5 years of MRD-negative PR patients who undergo auto-HCT followed by 3 years of maintenance rituximab
- Define OS and PFS at 2 and 5 years of MRD-indeterminate patients who undergo auto-HCT followed by 3 years of maintenance rituximab
- Describe the rate of complications in MCL patients undergoing maintenance rituximab following auto-HCT
- Determine the prognostic impact of MRD status at day 100 in MCL patients who were MRD-positive (CR and PR) prior to auto-HCT

Eligibility Criteria*

Screening (Step 0–Preregistration)

- ≥ 18 and ≤ 70 years of age
- Histologically confirmed MCL with cyclin D1 by immunohistochemical stains and/or t(11;14) by cytogenetics or FISH.
 - If patient has cyclin D1 negative MCL with classical morphology and an expression profile (including SOX11+) that is otherwise indistinguishable from MCL, communication with the study chair is required for consideration of enrollment
 - The proliferation rate, using Ki-67 or MIB-1, should also be determined, but is not required until step 1 registration

*When evaluating patients for this study, please refer to the full protocol for the complete list of eligibility criteria.

- In the opinion of the enrolling physician, thought to be a candidate for autologous stem cell transplantation
- May be about to begin, be receiving, or have completed induction therapy within 120 days prior to preregistration to step 0. No more than 300 days may have passed between the first day of induction therapy and preregistration to step 0
 - For patients who have completed induction therapy and have been restaged, restaging evaluation must show PR or CR status. Post-induction patients with evidence of clinical disease progression are not eligible for preregistration to step 0
 - Up to 2 regimens of therapy (conventional chemotherapy, antibody therapy, or an oral regimen) are allowed as long as a continuous response was

ongoing throughout therapy; PR must have been achieved

- Archived formalin-fixed paraffin embedded (FFPE) tumor tissue specimen from the original diagnostic biopsy available for submission to Adaptive Biotechnologies for ClonoSEQ® ID molecular marker identification of unique clonal immunoglobulin DNA sequence
(Note: peripheral blood collected prior to start of treatment with high disease burden is acceptable per protocol)
- No documented history of CNS involvement by MCL

Treatment Assignment (Step 1)

- Met eligibility criteria for screening step
- The proliferation rate, using Ki-67 or MIB-1 immunohistochemistry must be documented

Continued

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- Institution received results from Adaptive Biotechnologies as defined by: MRD indeterminate, ClonoSEQ did not identify any unique clonal immunoglobulin DNA sequence *or* ClonoSEQ identified unique clonal immunoglobulin DNA sequence and MRD assessment is completed
 - Up to 2 regimens of therapy (conventional chemotherapy, antibody therapy, or an oral regimen) are allowed, as long as a continuous response was ongoing throughout therapy
- Must have completed induction therapy within 150 days prior to registration to step 1 *and* no more than 300 days have elapsed from the first dose of induction chemotherapy (C1D1) given, until the last day of induction chemotherapy administered. For those assigned to arms A, C, or D, the date of transplant (day 0) must not be greater than 365 days after C1D1
 - Must have received at least 4 cycles of induction therapy
- Achieved radiologic CR or PR as defined by the Lugano criteria
- In the opinion of the enrolling physician, thought to be a candidate for autologous stem cell transplantation
- ECOG performance status of 0–2
- HIV-positive status is allowed, with specific disease requirements
- Disease-free ≥ 3 years of prior malignancies with the exception of adequately treated nonmelanoma skin cancer, adequately treated in situ carcinoma, melanoma in situ post wide local excision or Mohs surgery, low-grade prostate carcinoma (Gleason grade ≤ 6) managed with observation that has been stable for at least 6 months
- Use of effective contraception or abstinence during the trial and for 12 months post rituximab treatment
- Not pregnant or breastfeeding

