Version 03/03/22 (Add. #3)

NCI National Clinical Trials Network

EA4181

ECOG-ACRIN cancer research group

For Patients with Mantle Cell Lymphoma

EA4181 Available Through ECOG-ACRIN Cancer Research Group

A Randomized 3-Arm Phase II Study Comparing 1.) Bendamustine, Rituximab, and High Dose Cytarabine (BR/CR) 2.) Bendamustine, Rituximab, High Dose Cytarabine and Acalabrutinib (BR/CR-A), and 3.) Bendamustine, Rituximab and Acalabrutinib (BR-A) in Patients ≤ 70 Years Old with Untreated Mantle Cell Lymphoma

Patient Population

See Section 3.0 for Complete Eligibility Details

- Age ≥ 18 and ≤ 70; ECOG PS 0-2; adequate lab values
- Baseline measurements/evaluations obtained within 42 days of randomization; abnormal PET/CT scans may constitute evaluable disease; patients must have at least 1 objective measurable disease parameter by PET or CT (see protocol; measurable disease in the liver is required if it's the only site of lymphoma)
- MIPI score: calculated and entered in OPEN per protocol
- Must have untreated histologically confirmed mantle cell lymphoma, with cyclin D1 (BCL1) expression by immunohistochemical stains and/or t(11;14) by cytogenetics/FISH (see protocol for exception)
- Patients being treated with gastric reducing agents proton pump inhibitors must be switched to an alternative drug before starting acalabrutinib
- Patients with HIV/HBV/HCV are permitted per protocol
- Patients with known history/current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment using the NYHA Functional Classification; to be eligible for this trial, patients should be class 2B or better
- No patients that require treatment with a strong cytochrome P450 (CYP) 3A inhibitor; may not have received strong/moderate CYP3A inhibitors/inducers within 7 days prior to the first dose of study drug
- No patients with malabsorption syndrome/disease significantly affecting GI function, active bleeding/history of bleeding diathesis, uncontrolled AIHA/ITP, history of significant cerebrovascular disease/event within 6 months of the first dose of study drug, known active infections (per protocol) at study enrollment
- No warfarin/equivalent vitamin K antagonists with 7 days of first dose of study drug
- Able to provide FFPE tumor tissue/peripheral blood

Treatment Plan

See Section 5.0 for Complete Treatment Details

Cycle= 28 days; doses based on actual body weight

Arm A:

- Cycles 1, 2, 3: Rituximab 375 mg/m² IV Day 1 or 2; Bendamustine 90 mg/m² IV Day 1, 2
- Cycles 4, 5, 6: Rituximab 375 mg/m² IV Day 1 followed by Cytarabine 2000 mg/m² IV Q12 hours Day 1, 2 (for age 66-70 years: 1500 mg/m² IV Q12 hours days 1 and 2, starting dose)

Arm B:

- Cycles 1, 2, 3: Rituximab 375 mg/m² IV Day 1 or 2; Bendamustine 90 mg/m² IV Day 1, 2; Acalabrutinib 100 mg orally twice daily days 1-28
- Cycles 4, 5, 6: Rituximab 375 mg/m² IV Day 1 followed by Cytarabine 2000 mg/m² IV Q12 hours Day 1, 2 (for age 66-70 years: 1500 mg/m² IV Q12 hours days 1 and 2, starting dose); Acalabrutinib 100 mg orally twice daily days 1-7 and days 22-28

Arm C:

- Cycles 1-6: Rituximab 375 mg/m² IV Day 1 or 2; Bendamustine 90 mg/m² IV Day 1, 2; Acalabrutinib 100 mg orally twice daily on days 1-28

Notes:

- *Rituxan Hycela 1400 mg/23,400 UNITS SQ/ any approved biosimilar at the approved dose can be used instead of rituximab*
- *Cytarabine may be given on day 2 or 3 if rituximab is given as outpatient on day 1*
- *Rituximab/bendamustine/cytarabine administration is per institutional standard of care (see protocol for details)*
- *Acalabrutinib should be taken whole with water, with/without food. If a dose is missed by more than 3 hours, acalabrutinib should be skipped and the next dose taken at the regular scheduled time*
- *See protocol for criteria for initiating a new course of treatment (on scheduled day 1 of a new cycle)*

Study Chair:
Nina Wagner-Johnston, MD

SWOG Co-Chair:
Stephen Spurgeon, MD

Alliance Co-Chair:
Kami Maddocks, 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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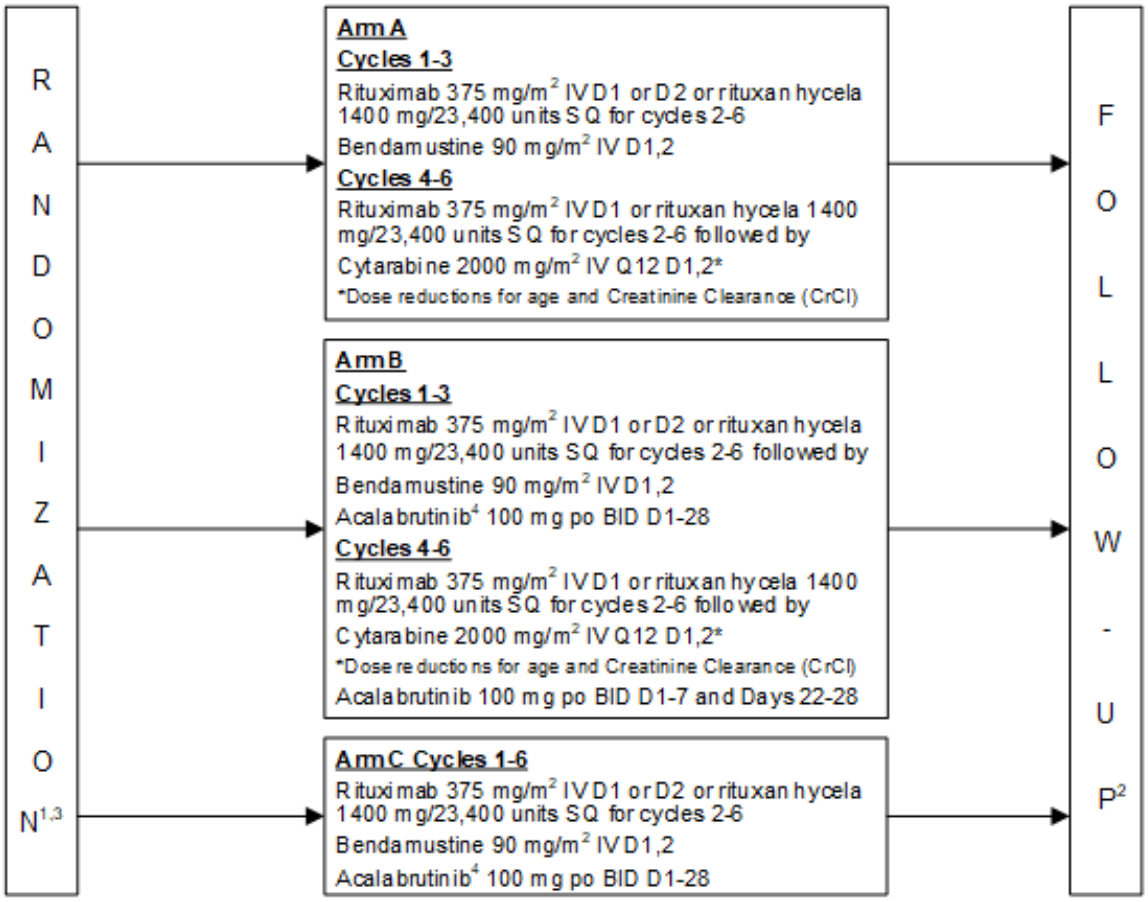
Schema



1 Cycle = 28 days

Accrual Goal: 369

1. Stratify using the MIPI risk score: high vs. intermediate vs. low. Diagnositc FFPE tumor tissue (or involved bone marrow) must be sent to Adaptive within 60 days of enrollment.
2. Patients will be followed per Section 5.5. MRD will be assessed cycle 6, d28 (+ 5 weeks) after completion of study treatment and specimen submissions should follow guidelines in Section 7.2.
3. Randomization will occur 1:1:1 between Arms A, B, and C.
4. If treatment initiation is urgent and acalabrutinib is not available for cycle 1, treatment with bendamustine and rituximab may begin up to 4 days prior to acalabrutinib start.