

Oncology Clinical Pathways

Mantle Cell Lymphoma

March 2025 – V1.2025



Choose **VA**



SHOULDER to SHOULDER
Every Step of the Way

VA



U.S. Department
of Veterans Affairs

Table of Contents

[Presumptive Conditions](#).....3

[Mantle Cell Lymphoma – Stage I and Contiguous Stage II](#).....4

[Mantle Cell Lymphoma – Bulky Stage II, Stage III, and Stage IV](#).....5

[Mantle Cell Lymphoma – Relapsed or Refractory](#).....6

[Mantle Cell Lymphoma – Molecular Testing Table](#).....7

Presumptive Conditions – Mantle Cell Lymphoma

VA automatically presumes that certain disabilities were caused by military service. This is because of the unique circumstances of a specific Veteran's military service. If a presumed condition is diagnosed in a Veteran within a certain group, they can be awarded disability compensation.

Atomic Veterans – Exposure to Ionizing Radiation

- Lymphomas, other than Hodgkin's disease

Gulf War and Post 9/11 Veterans

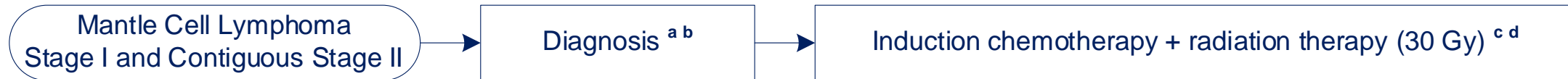
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if the patient served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- Lymphoma of any type

* The Southwest Asia theater of operations refers to Iraq, Kuwait, Saudi Arabia, the neutral zone between Iraq and Saudi Arabia, Bahrain, Qatar, the United Arab Emirates, Oman, the Gulf of Aden, the Gulf of Oman, the Persian Gulf, the Arabian Sea, the Red Sea, and the airspace above these locations.

For more information, please visit [U.S. Department of Veterans Affairs - Presumptive Disability Benefits \(va.gov\)](https://www.va.gov/presumptive-disability-benefits/)

Mantle Cell Lymphoma – Stage I and Contiguous Stage II



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

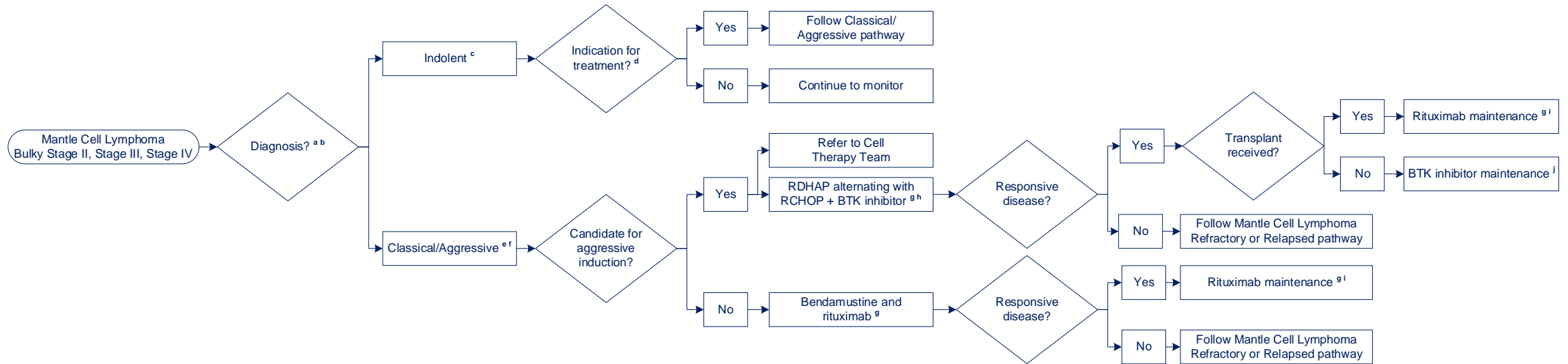
^a **Diagnosis** requires tissue morphology and immunophenotype (IHC or flow cytometry) including CD3, CD20, and cyclin D1; SOX11 IHC and/or FISH for t(11;14) *IGH::CCND1* can also be performed at pathologist discretion to aid in diagnosis; for prognostic purposes, Ki-67 IHC should also be performed (prognostically significant cutoff of 30%), as well as molecular testing for TP53 mutations and FISH for del 17p (TP53)

^b **Testing** to include: HIV, Hepatitis, LDH, uric acid, CBC with diff, CMP, PET, bone marrow biopsy to confirm limited state and is encouraged in other scenarios; endoscopy indicated to confirm limited stage disease or for GI symptoms or iron deficiency anemia; LP may be indicated for CNS symptoms

^c **Induction Chemotherapy** is appropriate in younger, fit patients with more aggressive presentations; bendamustine/rituximab is the treatment of choice

^d **Rituximab** Hepatitis B serologies prior to starting anti-CD20 antibody therapy; consider HBV DNA if HBsAg or HBcAb positive; prescribe entecavir if HBsAg or HBcAb positive

Mantle Cell Lymphoma – Bulky Stage II, Stage III, Stage IV



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

^a **Diagnosis** requires tissue morphology and immunophenotype (IHC or flow cytometry) including CD3, CD20, and cyclin D1; SOX11 IHC and/or FISH for t(11;14) *IGH::CCND1* can also be performed at pathologist discretion to aid in diagnosis; for prognostic purposes, Ki-67 IHC should also be performed (prognostically significant cutoff of 30%), as well as molecular testing for TP53 mutations and FISH for del 17p (TP53)

^b **Testing** to include HIV, Hepatitis, LDH, uric acid, CBC with diff, CMP, PET, bone marrow biopsy to confirm limited state and is encouraged in other scenarios; endoscopy indicated to confirm limited stage disease or for GI symptoms or iron deficiency anemia; LP may be indicated for CNS symptoms; evaluate cardiovascular risk factors and baseline LVEF (with ECHO or MUGA)

^c **Indolent** combination of clinical and pathological presentation usually includes leukemic non-nodal CLL like presentation with low tumor burden and Ki-67 <10%; generally must be CD5 positive and cyclin D1 positive and frequently SOX 11 negative with clinical observation stability overtime

^d **Indications for Treatment** include anemia Hgb <10 g/dL, platelets <100,000/mm³, thrombocytopenia/anemia must be non-immune and not related to alternate causes, B-symptoms, and symptomatic adenopathy; consider cross-sectional imaging prior to initiation of therapy

^e **Classical/Aggressive** blastoid variant has poor prognosis

^f **TP53 Mutations** confers a poor prognosis and there is no standard therapy recommended; auto transplant might not be a good idea for the patients with TP53 mutation; consolidation may not be effective for them; consider clinical trial or alternate therapies that incorporate novel agents

^g **Rituximab Supportive Care** Hepatitis B serologies prior to starting anti-CD20 antibody therapy (e.g. rituximab); consider HBV DNA if HBsAg or HBcAb positive; prescribe entecavir if HBsAg or HBcAb positive

^h **RDHAP Regimen** should be used with caution in patients on anticoagulation or who are at high-risk for bleeding

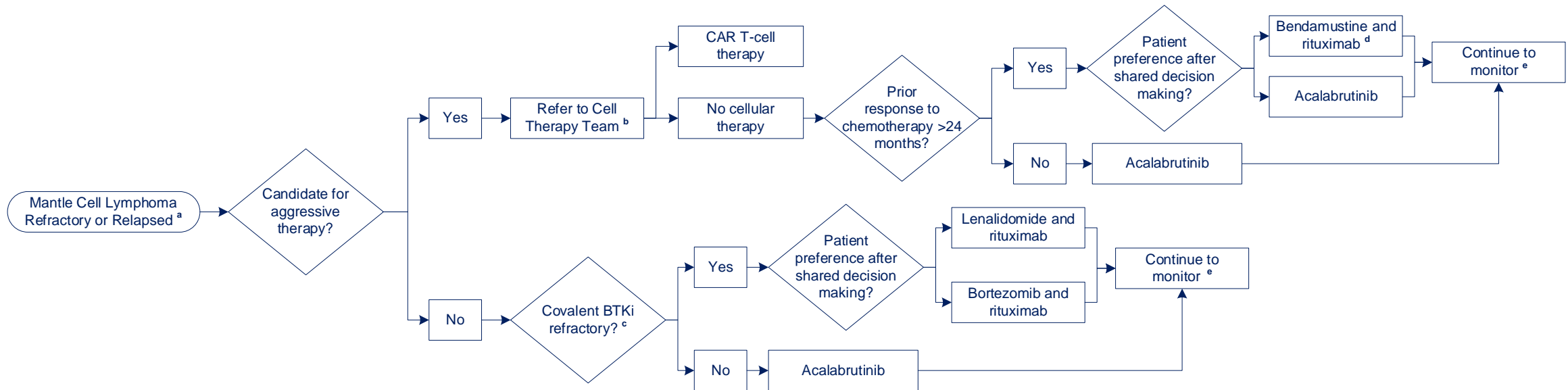
ⁱ **Rituximab Maintenance** different durations of rituximab have been studied; however, the maximum duration recommended is 3 years

^j **BTK Inhibitor maintenance** duration recommended is two years

RDHAP rituximab, dexamethasone, cytarabine, platinum agent (cisplatin, carboplatin, oxaliplatin)

RCHOP rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone

Mantle Cell Lymphoma – Relapsed or Refractory



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

^a **Refractory or Relapsed** confirmed by excisional biopsy

^b **Refer to Cell Therapy Team** for bridging therapies prior to CAR T-cell or autologous collection

^c **Covalent BTKi** acalabrutinib, ibrutinib, or zanubrutinib

^d **Bendamustine** if not used before

^e **Continue to Monitor** consider pirtobrutinib for third line Mantle cell lymphoma and including prior covalent BTKi

BTKi Bruton Tyrosine Kinase Inhibitor

CAR Chimeric Antigen Receptor

SCT Stem Cell Transplantation

Mantle Cell Lymphoma – Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Mantle Cell Lymphoma (MCL)	IHC	Cyclin D1 (CCND1), TP53, SOX11, Ki-67	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	FISH	Translocations t(11;14) Test for deletion 17p	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Molecular Testing	TP53 mutation	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood



Choose **VA**



SHOULDER to SHOULDER
Every Step of the Way

VA



U.S. Department
of Veterans Affairs

Mantle Cell Lymphoma – References

1. Center. FDA approves acalabrutinib with bendamustine and rituximab. U.S. Food and Drug Administration. Published 2025. <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-acalabrutinib-bendamustine-and-rituximab-previously-untreated-mantle-cell-lymphoma>
2. Collins TR. Ibrutinib-Rituximab Outperforms Chemotherapy in Front-Line MCL, Trial Finds. Ashpublications.org. Published December 5, 2024. Accessed February 14, 2025. <https://ashpublications.org/ashclinicalnews/news/8301/Ibrutinib-Rituximab-Outperforms-Chemotherapy-in>
3. Dreyling M, Doorduijn J, Giné E, et al. Ibrutinib combined with immunochemotherapy with or without autologous stem-cell transplantation versus immunochemotherapy and autologous stem-cell transplantation in previously untreated patients with mantle cell lymphoma (TRIANGLE): a three-arm, randomised, open-label, phase 3 superiority trial of the European Mantle Cell Lymphoma Network. Lancet. Published online May 1, 2024. doi:[https://doi.org/10.1016/s0140-6736\(24\)00184-3](https://doi.org/10.1016/s0140-6736(24)00184-3)
4. Dreyling M, Mayer J, Belada D, et al. High-Risk Subgroups and MRD: An Updated Analysis of the Phase 3 ECHO Trial of Acalabrutinib with Bendamustine/Rituximab in Previously Untreated Mantle Cell Lymphoma. Blood. 2024;144(Supplement 1):1626-1626. doi:<https://doi.org/10.1182/blood-2024-200290>
5. Kumar A, Soumerai J, Abramson JS, et al. Zanubrutinib, obinutuzumab, and venetoclax for first-line treatment of mantle cell lymphoma with a TP53 mutation. Blood. 2025;145(5):497-507. doi:<https://doi.org/10.1182/blood.2024025563>