

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

## PATHOLOGIC DIAGNOSIS

### ESSENTIAL:

- Hematopathology review of all slides with at least one tumor paraffin block. Hematopathology confirmation of classic versus aggressive variant of MCL (blastoid/pleomorphic). Re-biopsy if consult material is non-diagnostic.
- Adequate immunophenotype to confirm diagnosis<sup>1</sup>
  - Paraffin panel<sup>2</sup> **or** flow cytometry immunophenotyping: kappa/lambda light chains, CD5, CD10, CD19, CD20, CD23, FMC-7, CD200, and CD43 **and**
  - Ki-67 (proliferation rate)

### OF USE IN CERTAIN CIRCUMSTANCES:

- Molecular genetic analysis
  - Somatic hyper-mutation for IGHV gene rearrangement and mutation status
  - *TP53*                      ◦ *NSD2*
  - *NOTCH1*                    ◦ *BTK*
  - *NOTCH2*                    ◦ *KMT2D*
- Immunohistochemistry for *SOX-11* and *CD23*
- FISH to detect t(11;14)(q13;q32)/*CCND1::IGH*, *TP53*, and *MYC*

### STRONGLY RECOMMENDED:

- Fine needle aspiration (FNA) or core biopsy for tissue banking by protocol

FISH = fluorescence in situ hybridization

<sup>1</sup> Immunophenotype: CD5+, CD20+, CD43+, CD200-/+ , ROR1+/-, CD23-/+ , cyclin D1+.

**Note:** Some cases of Mantle Cell Lymphoma may be CD5-, CD10+, or CD23+.

If the diagnosis is suspected, cyclin D1 staining or FISH to demonstrate t(11;14)(q13;q32) should be performed.

<sup>2</sup> Upon tissue availability, consider Pan B-cell marker (CD19, CD20, PAX5), CD3, CD5, CD10, and cyclin D1.

<sup>3</sup> See [Physical Activity](#), [Nutrition](#), and [Tobacco Cessation](#) algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

<sup>4</sup> Obtain 4-6 biopsies from each of the following areas during EGD/colonoscopy: duodenum including duodenal bulb, gastric antrum, gastric body, terminal ileum, throughout the colon including right, left and transverse, rectum

## INITIAL EVALUATION

### ESSENTIAL:

- Physical exam: attention to node-bearing areas, including Waldeyer's ring, size of liver and spleen, and patient's age
- Performance status (ECOG)
- B symptoms (fever, drenching night sweats, unintentional weight loss)
- CBC with differential, LDH, BUN, creatinine, albumin, AST, ALT, alkaline phosphatase, total bilirubin, indirect bilirubin, serum magnesium, serum calcium, uric acid, aPTT, prothrombin time and INR
- Urinalysis
- IgM, IgG, IgA
- Screening for HIV 1 and 2, hepatitis B and C (HBcAb, HBsAg, HCVAb)
- Beta-2 microglobulin (B2M)
- Chest x-ray, PA and lateral
- Bone marrow unilateral biopsy with unilateral aspirate
- PET/CT with contrast (preferred)
  - CT neck, chest, abdomen and pelvis with contrast (if PET-CT is not feasible)
- Lifestyle risk assessment<sup>3</sup>

### OF USE IN SELECTED CASES:

- Protein electrophoresis
- EGD/colonoscopy with segmental biopsies<sup>4</sup>
- Plain bone radiographs and bone scan                      • Lumbar puncture
- CT head with contrast or MRI brain                            • Colonoscopy
- Discuss fertility preservation options and sperm banking for patients of child bearing potential                      • Urine pregnancy test
- Referral(s) as indicated:
  - Cardiology to screen for cardiac related comorbidities specially for atrial fibrillation, hypertension, and major EKG abnormalities
  - Genetics to screen for family history of hematologic or other cancers
  - Dermatology to screen for secondary skin cancers

Induction Therapy for untreated MCL see [Page 2](#)

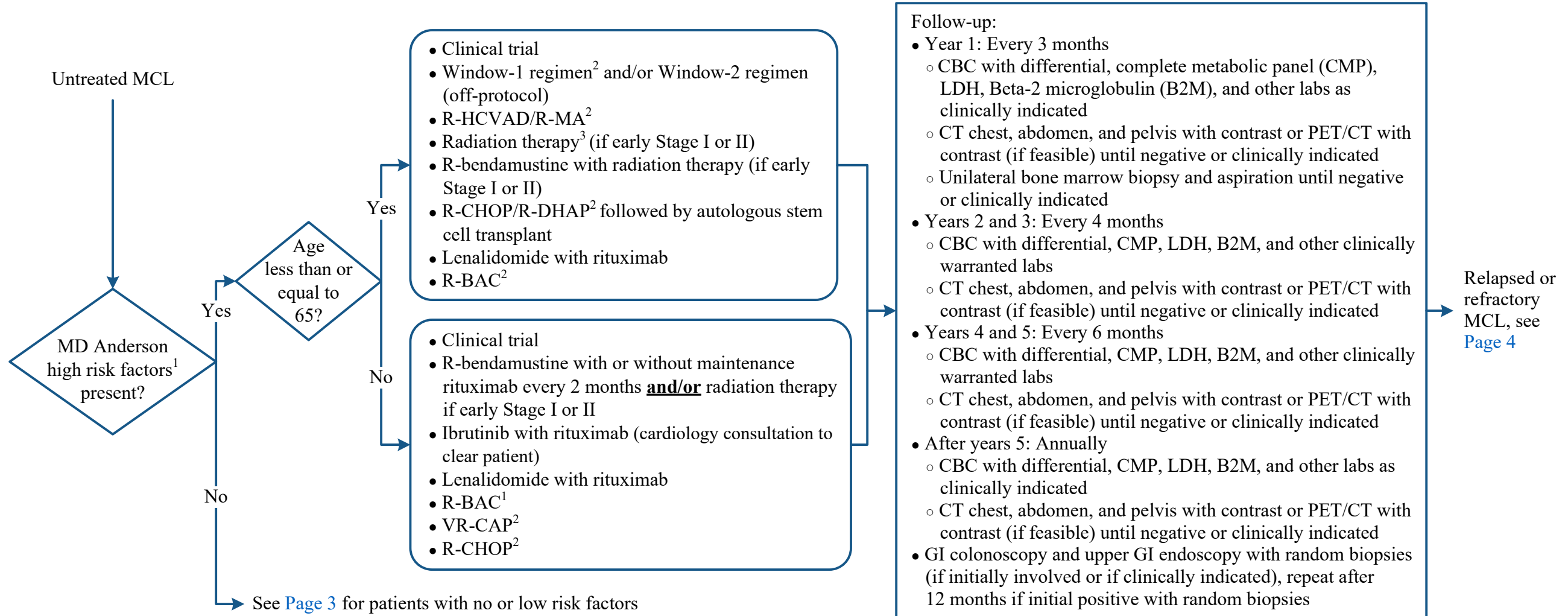
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**Note:** Consider Clinical Trials as treatment options for eligible patients.

## PRESENTATION

## INITIAL THERAPY

## FOLLOW-UP



<sup>1</sup> High Risk factors: Blastoid/pleomorphic histology, *TP53* mutation or *del17p* by FISH, complex karyotype, MYC positive by FISH, bulky tumor > 7 cm and spleen > 20 cm, Ki-67 ≥ 30% in tissue biopsy

<sup>2</sup> Chemotherapy regimen abbreviations, see Appendix A

<sup>3</sup> The recommended radiation dose is 24 Gy

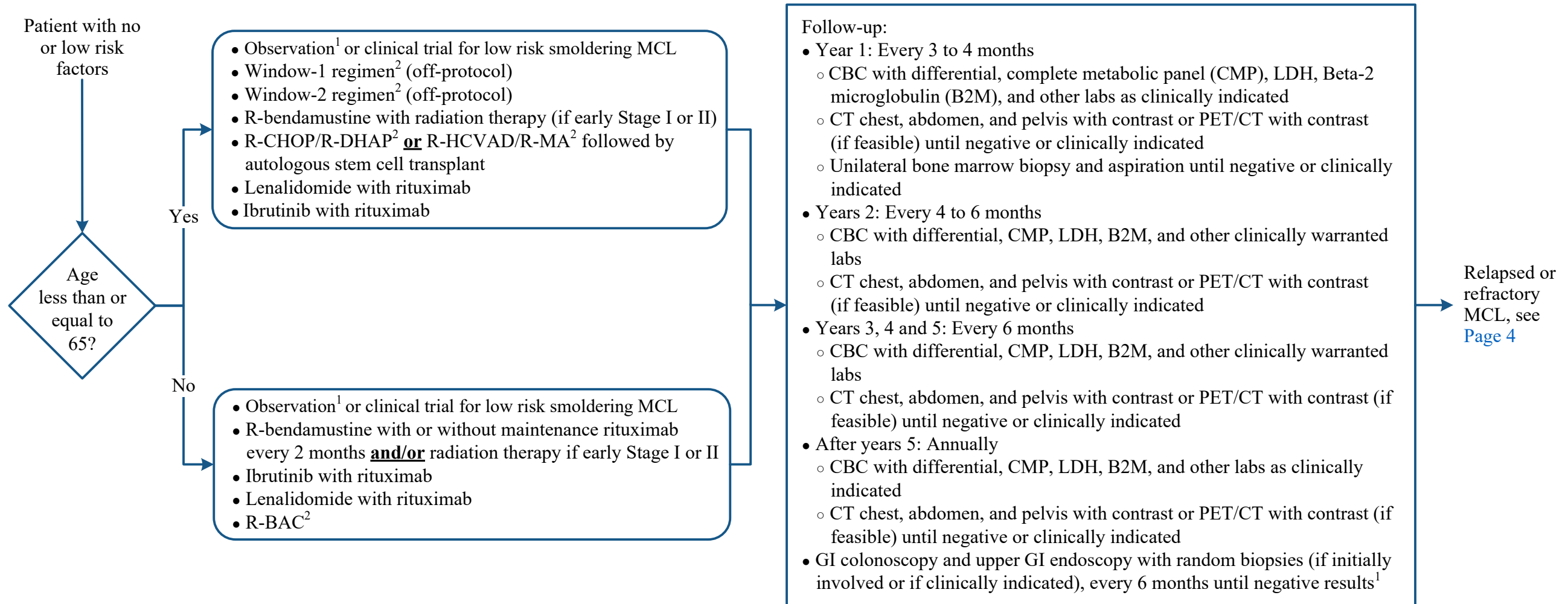
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## PRESENTATION

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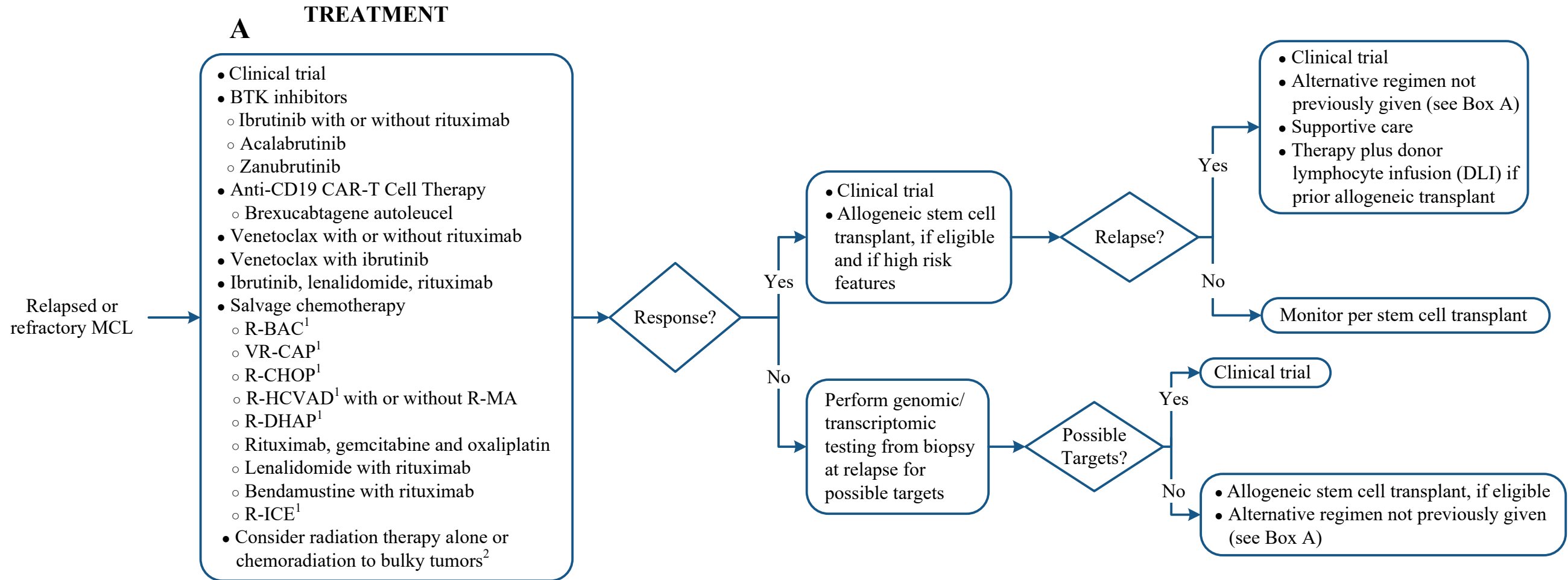


<sup>1</sup> Initial GI scopes with biopsies may be needed to help decide on observation or therapy

<sup>2</sup> Chemotherapy regimen abbreviations, see [Appendix A](#)

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**Note:** Consider Clinical Trials as treatment options for eligible patients.



<sup>1</sup> Chemotherapy regimen abbreviations, see [Appendix A](#)

<sup>2</sup> The preferred initial radiation dose is 4 Gy. Consider higher dose of 20-24 Gy for non-responders to 4 Gy.

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## APPENDIX A: Chemotherapy Regimen Abbreviations

**Window-1:** ibrutinib and rituximab followed by 4 cycles of R-HCVAD/R-MA

**Window-2:** ibrutinib-rituximab and venetoclax (IRV) followed by risk stratified R-HCVAD

- Low Risk: only IRV maintenance for up to 2 years
- Intermediate Risk: 2 cycles of R-HCVAD/R-MA followed by IRV maintenance up to 2 years
- High Risk: 4 cycles of R-HCVAD/R-MA followed by IRV maintenance up to 2 years

**R-HCVAD:** rituximab, cyclophosphamide, vincristine, doxorubicin, dexamethasone, and (mesna); alternating with R-MA

**R-MA:** rituximab, methotrexate, and cytarabine; alternating with R-HCVAD

**R-CHOP:** rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone

**R-DHAP:** rituximab, dexamethasone, cytarabine, and cisplatin

**R-BAC:** rituximab, bendamustine, and low-dose cytarabine

**R-ICE:** rituximab, ifosfamide, carboplatin, and etoposide

**VR-CAP:** bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone

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## DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Lymphoma Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

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