Mantle Cell Lymphoma (MCL)

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

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
  - Paraffin panel: CD3, CD5, CD10, pan B-cell marker (CD20 or PAX5), cyclin D1[1], SOX11, Ki67, and p53
  - Flow cytometry immunophenotyping: CD5, CD10, CD19, CD20, CD23, CD43, CD200, and kappa/lambda light chains

USE IN CERTAIN CIRCUMSTANCES:

- Molecular genetic analysis
  - Somatic hyper-mutation for IGHV gene rearrangement and
  - Mutation analysis: *BTK, KMT2D, NOTCH1, NOTCH2, NSD2,* and *TP53*
- Immunohistochemistry: MYC protein
- FISH to detect t(11;14)(q13;q32)[1]/*IGH::CCND1,TP53*, and *MYC*

STRONGLY RECOMMENDED:

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

FISH = fluorescence in situ hybridization
ECOG = Eastern Cooperative Oncology Group

[1] Some cases of MCL 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.
[2] See Physical Activity, Nutrition, and Tobacco Cessation Treatment algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
[3] 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
- ECOG performance status
- B symptoms (unexplained fever > 38°C during the previous month; recurrent drenching night sweats during the previous month; weight loss > 10% of body weight ≤ 6 months of diagnosis)
- CBC with differential, basic metabolic panel (BMP) with total calcium, hepatic function panel, magnesium, calcium, LDH, uric acid, aPTT, prothrombin time and INR
- Urinalysis
- IgM, IgG, IgA
- Beta-2 microglobulin (B2M)
- Screening for HIV 1 and 2, hepatitis B and C (HBcAb, HBsAg, HCVAb) (refer to Hepatitis B Virus (HBV) Screening and Management and Hepatitis C Virus (HCV) Screening algorithms)
- Bone marrow unilateral biopsy with unilateral aspirate
  - Clonality for minimal residual disease tracking
- Baseline EKG and 2-D echocardiogram
- Chest x-ray, PA and lateral
- PET/CT with contrast (preferred)
  - CT neck, chest, abdomen and pelvis with contrast (if PET-CT is not feasible)
- Lifestyle risk assessment[2]

OF USE IN SELECTED CASES:

- Protein electrophoresis
- EGD/colonoscopy with segmental biopsies[3] and antinuclear antibody
- Plain bone radiographs and bone scan
- Lumbar puncture
- Colonoscopy
- Urine pregnancy test
- CT head with contrast or MRI brain
- Discuss fertility preservation options and sperm banking for patients of child bearing potential (refer to Fertility Preservation Prior to Cancer Treatment algorithm)
- Referral(s) as indicated:
  - Cardiology referral if history of arrythmias, hypertension, coronary artery disease, cardiomyopathy/ heart failure, or significant EKG abnormalities such as left bundle branch block, prior myocardial infarction, atrial enlargement or heart block
  - Genetics referral if family history of hematologic or other cancers
  - Dermatology referral if secondary skin cancers

Induction Therapy for untreated MCL see Page 2

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PRESENTATION

Untreated MCL

At least one MD Anderson high risk factor[1] present?

Yes

Discuss Goal Concordant Care (GCC) with patient or if clinically Indicated, with Patient Representative[2]

Age ≤ 65 years?

No

See Page 3 for patients without high risk factors[1] **and** with lymphoma symptoms[6]

INITIAL THERAPY

Yes

- Clinical trial **or**
- Window-1 regimen[3] (off-protocol)or Window-2 regimen[3] (off-protocol) **or**
- R-HCVAD/R-MA[3] **or**
- R-bendamustine **or**
- R-BAC[3] **or**
- LyMA regimen[3] **or**
- TRIANGLE regimen[3] **or**
- Radiation therapy[4] if early Stage I or II
- Perform leukapheresis if the absolute lymphocyte count > 30 K/microliter in leukemic phase MCL

No

- Clinical trial
- Acalabrutinib or zanubrutinib[5] with rituximab (preferred)
- R-bendamustine **or**
- R-BAC[3] **or**
- VR-CAP[3] **or**
- Lenalidomide with rituximab
- Radiation therapy[4] if early Stage I or II
- Perform leukapheresis if the absolute lymphocyte count > 30 K/microliter in leukemic phase MCL

CONSOLIDATION/MAINTENANCE THERAPY

- Maintenance with covalent BTK inhibitor and rituximab every 2 months for 2 years with or without venetoclax
- Consider high dose therapy (HDT) followed by autologous stem cell transplant (ASCT) in the appropriate clinical setting

Maintenance with covalent BTK inhibitor and rituximab every 2 months for 2 years

- See Page 4 for Surveillance
- See Page 5 for Relapsed or Refractory MCL

BTK = bruton tyrosine kinase

[1] High risk factors include blastoid/pleomorphic histology, *TP53* mutation or *del17p* by FISH, complex karyotype, *MYC* positive by FISH, bulky tumor > 5 cm and spleen > 20 cm, Ki-67 ≥ 30% in tissue biopsy

[2] GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).

[3] See Appendix A for chemotherapy abbreviations and regimens

[4] The recommended radiation dose is 24 Gy

[5] Ibrutinib may be substituted for acalabrutinib or zanubrutinib (Cardiology consultation to clear patient)

[6] Consider observation in patients without high risk factors **and** with no lymphoma symptoms

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PRESENTATION

Patients without high risk factors[1] **and** with lymphoma symptoms[2]

Age ≤ 65 years?

INITIAL THERAPY

Yes

- Clinical trial **or**
- Observation[3] for low risk smoldering MCL **or**
- Acalabrutinib or zanubrutinib with rituximab (preferred) **or**
- Window-1 regimen[4] (off-protocol) and/or Window-2 regimen[4] (off-protocol) **or**
- R-bendamustine
- Radiation therapy if early Stage I or II

No

- Clinical trial **or**
- Observation[3] for low risk smoldering MCL **or**
- Acalabrutinib or zanubrutinib with rituximab (preferred) **or**
- R-bendamustine **or**
- R-BAC[4]
- Radiation therapy if early Stage I or II

CONSOLIDATION/MAINTENANCE THERAPY

Maintenance with covalent BTK inhibitor and rituximab every 2 months for 2 years with or without venetoclax

- See Page 4 for Surveillance
- See Page 5 for Relapsed or Refractory MCL

[1] High risk factors include blastoid/pleomorphic histology, *TP53* mutation or *del17p* by FISH, complex karyotype, *MYC* positive by FISH, bulky tumor > 5 cm and spleen > 20 cm, Ki-67 ≥ 30% in tissue biopsy
[2] Consider observation in patients without high risk factors **and** with no lymphoma symptoms
[3] Initial GI scopes with biopsies may be needed to help decide on observation or therapy
[4] See Appendix A for chemotherapy abbreviations and regimens

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

SURVELLIANCE

Diagnostics	MD Anderson High Risk Factors[1]	Without High Risk Factors[1] and with no lymphoma symptoms
CBC with differential, BMP with total calcium, hepatic function panel, LDH, Beta-2 microglobulin (B2M), and other labs as clinically indicated CT Abdomen/Pelvis (with and without contrast) or PET/CT with contrast (if feasible)	Every 3 months for Year 1, then every 4 months for Years 2-3, then every 6 months for Years 4-5, then annually	Every 3-4 months for Year 1, then every 4-6 months for Year 2, then every 6 months for Years 3-5, then annually
Unilateral bone marrow biopsy and aspiration	Every 3 months for Year 1 until negative or as clinically indicated	Every 3 months for Year 1 until negative or as clinically indicated
GI colonoscopy and upper GI endoscopy with random biopsies (if initially involved or if clinically indicated)[2]	At 6 months if initial positive with random biopsies or as clinically indicated	At 12 months if initial positive with random biopsies or as clinically indicated

[1] High risk factors include blastoid/pleomorphic histology, *TP53* mutation or *del17p* by FISH, complex karyotype, *MYC* positive by FISH, bulky tumor > 5 cm and spleen > 20 cm, Ki-67 ≥ 30% in tissue biopsy
[2] Initial GI scopes with biopsies may be needed to help decide on observation or therapy

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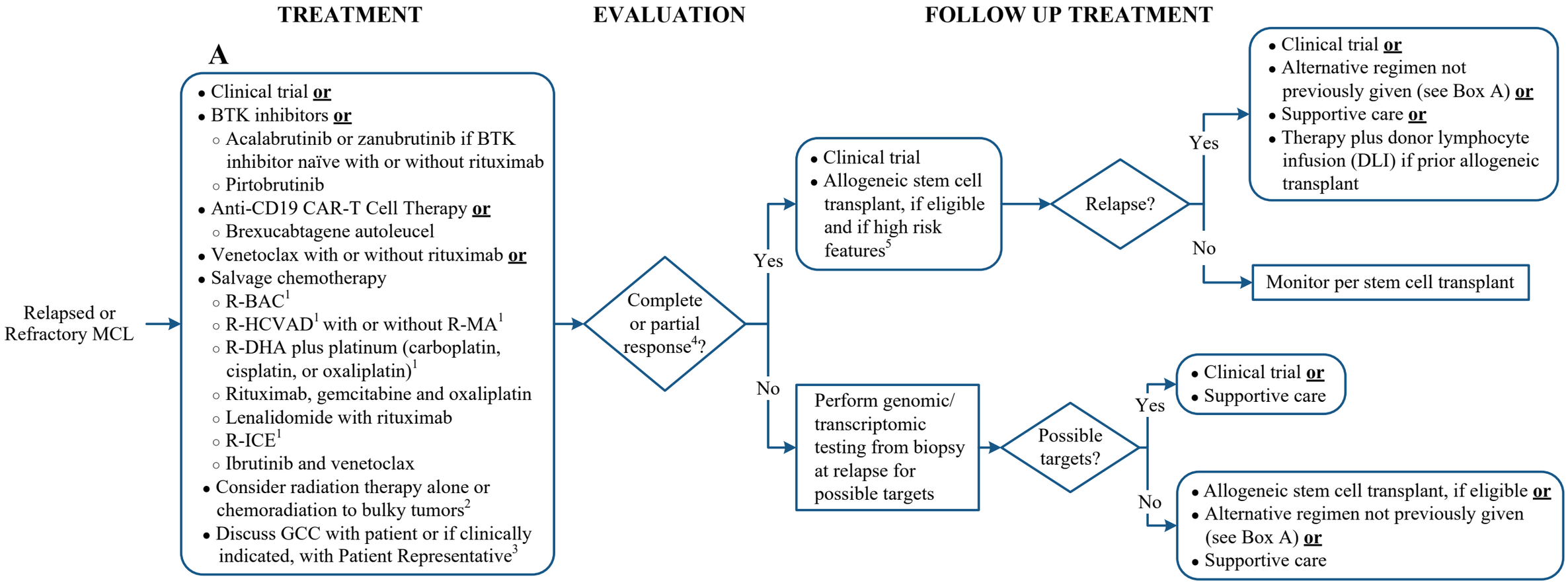
Note: Consider Clinical Trials as treatment options for eligible patients.



[1] See Appendix A for chemotherapy abbreviations and regimens

[2] The preferred initial radiation dose is 4 Gy. Consider higher dose of 20-24 Gy for non-responders to 4 Gy.

[3] GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).

[4] For response assessment, refer to: Cheson, B. D., Fisher, R. I., Barrington, S. F., Lister, T. A., Cavalli, F., Zucca, E., & Schwartz, L. H. (2014). Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: The Lugano classification. *Journal of Clinical Oncology*, *32*(27), 3059-3067. doi:10.1200/JCO.2013.54.8800

[5] Includes patients who are physically fit for stem cell transplantation with TP53 mutation and/or CNS relapse

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APPENDIX A: Chemotherapy Abbreviations and Regimens

Window-1: ibrutinib[1] (560 mg PO daily) and rituximab[2] (IV weekly for the first 4 weeks and then on Day 1 of Cycles 3-12) for 12 cycles followed by R-HCVAD alternating with R-MA (total 4 cycles)
Window-2: ibrutinib[1] and rituximab[2] (see regimen above) plus venetoclax (IRV) starting Cycle 5 (dose escalation of 20 mg, 50 mg, 100 mg, 200 mg, and then 400 mg) followed by risk stratified consolidation/maintenance

- 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[2], hyperfractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone; alternating with R-MA
R-MA: rituximab[2], methotrexate, and cytarabine; alternating with R-HCVAD
R-CHOP: rituximab[2], cyclophosphamide, doxorubicin, vincristine, and prednisone
R-DHA plus platinum: rituximab[2], dexamethasone, cytarabine, and platinum (carboplatin, cisplatin, or oxaliplatin)
R-BAC: rituximab[2], bendamustine, and low-dose cytarabine
R-ICE: rituximab[2], ifosfamide, carboplatin, and etoposide
VR-CAP: bortezomib, rituximab[2], cyclophosphamide, doxorubicin, and prednisone
LyMA: R-DHA plus platinum (carboplatin, cisplatin or oxaliplatin) for 4 cycles, followed by R-CHOP for non-PET complete response
TRIANGLE: R-CHOP plus covalent BTK inhibitor alternating with R-DHA plus platinum (carboplatin, cisplatin or oxaliplatin)

[1] May substitute ibrutinib with acalabrutinib or zanubrutinib as indicated for cardiac safety concerns if financially approved; otherwise ibrutinib 420 mg PO daily may be substituted after cardiac assessment
[2] Recommend delayed or slow infusion of rituximab with absolute lymphocyte count > 25 K/microliter

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SUGGESTED READINGS

Aukema, S. M., Hoster, E., Rosenwald, A., Canoni, D., Delfau-Larue, M. H., Rymkiewicz, G., … Dreyling, M. (2018). Expression of TP53 is associated with the outcome of MCL independent of MIPI and Ki-67 in trials of the European MCL Network. *Blood, 131*(4), 417-420. doi:10.1182/blood-2017-07-797019

Beà, S., Valdés-Mas, R., Navarro, A., Salaverria, I., Martín-Garcia, D., Jares, P., … Conde, L. (2013). Landscape of somatic mutations and clonal evolution in mantle cell lymphoma. *Proceedings of the National Academy of Sciences, 110*(45), 18250-18255. doi:10.1073/pnas.1314608110

Carvajal-Cuenca, A., Sua, L. F., Silva, N. M., Pittaluga, S., Royo, C., Song, J. Y., … Delabie, J. (2012). In situ mantle cell lymphoma: Clinical implications of an incidental finding with indolent clinical behavior. *Haematologica, 97*(2), 270-278. doi:10.3324/haematol.2011.05262

Cheson, B. D., Fisher, R. I., Barrington, S. F., Lister, T. A., Cavalli, F., Zucca, E., & Schwartz, L. H. (2014). Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: The Lugano classification. *Journal of Clinical Oncology*, *32*(27), 3059-3067. doi:10.1200/JCO.2013.54.8800

Dabaja, B. S., Tsang, R., Qi, S., Allen, P., Hodgson, D. C., Ricardi, U., Hoppe, R. T., … Constine, L. (2013). Either combined-modality or radiotherapy alone provide favorable outcome in stage I-II mantle cell lymphoma: A report of 82 patients from the International Lymphoma Radiation Oncology Group (ILROG). *Blood, 122*(21), 4292. doi:10.1093/annonc/mdx334

Determann, O., Hoster, E., Ott, G., Wolfram Bernd, H., Loddenkemper, C., Leo Hansmann, M., … Klapper, W. (2008). Ki-67 predicts outcome in advanced-stage mantle cell lymphoma patients treated with anti-CD20 immunochemotherapy: Results from randomized trials of the European MCL Network and the German Low Grade Lymphoma Study Group. *Blood, 111*(4), 2385-2387. doi:10.1182/blood-2007-10-117010

Dreyling, M., Doorduijn, J. K., Gine, E., Jerkeman, M., Walewski, J., Hutchings, M., … Hoster, E. (2022). Efficacy and safety of ibrutinib combined with standard first-line treatment or as substitute for autologous stem cell transplantation in younger patients with mantle cell lymphoma: Results from the randomized triangle trial by the European MCL Network. *Blood, 140* (Supplement 1), 1-3. doi:10.1182/blood-2022-163018

Eskelund, C. W., Dahl, C., Hansen, J. W., Westman, M., Kolstad, A., Pedersen, L. B., … Pedersen, A. (2017). TP53 mutations identify younger mantle cell lymphoma patients who do not benefit from intensive chemoimmunotherapy. *Blood, 130*(17), 1903-1910. doi:10.1182/blood-2017-04-779736

Eskelund, C. W., Kolstad, A., Jerkeman, M., Räty, R., Laurell, A., Eloranta, S., … Eriksson, M. (2016). 15-year follow-up of the Second Nordic Mantle Cell Lymphoma trial (MCL 2): Prolonged remissions without survival plateau. *British Journal of Haematology, 175*(3), 410-418. doi:10.1111/bjh.14241

Fisher, R. I., Bernstein, S. H., Kahl, B. S., Djulbegovic, B., Robertson, M. J., de Vos, S., … Goy, A. (2006). Multicenter phase II study of bortezomib in patients with relapsed or refractory mantle cell lymphoma. *Journal of Clinical Oncology, 24*(30), 4867-4874. doi:10.1200/JCO.2006.07.9665

Greenwell, I. B., Staton, A. D., Lee, M. J., Switchenko, J. M., Saxe, D. F., Maly, J. J., … Danilov, A. V. (2018). Complex karyotype in patients with mantle cell lymphoma predicts inferior survival and poor response to intensive induction therapy. *Cancer, 124*(11), 2306-2315. doi:10.1002/cncr.31328

Hoster, E., Dreyling, M., Klapper, W., Gisselbrecht, C., van Hoof, A., Kluin-Nelemans, H. C., … Unterhalt, M. (2008). A new prognostic index (MIPI) for patients with advanced-stage mantle cell lymphoma. *Blood, 111*(2), 558-565. doi:10.1182/blood-2007-06-095331

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SUGGESTED READINGS - continued

Hoster, E., Rosenwald, A., Berger, F., Bernd, H. W., Hartmann, S., Loddenkemper, C., … Kodet, R. (2016). Prognostic value of Ki-67 index, cytology, and growth pattern in mantle-cell lymphoma: Results from randomized trials of the European Mantle Cell Lymphoma Network. *Journal of Clinical Oncology, 34*(12), 1386-1394. doi:10.1200/JCO.2015.63.8387

Jain, P., Dreyling, M., Seymour, J. F., & Wang, M. (2020). High-risk mantle cell lymphoma: Definition, current challenges, and management. *Journal of Clinical Oncology, 38*(36), 4302-4316. doi:10.1200/JCO.20.02287

Jain, P., Kanagal-Shamanna, R., Zhang, S., Ahmed, M., Ghorab, A., Zhang, L., … Gong, T. (2018). Long-term outcomes and mutation profiling of patients with mantle cell lymphoma (MCL) who discontinued ibrutinib. *British Journal of Haematology, 183*(4), 578-587. doi:10.1111/bjh.15567

Jain, P., Romaguera, J., Srour, S. A., Lee, H. J., Hagemeister, F., Westin, J., … Nastoupil, L. (2018). Four-year follow-up of a single arm, phase II clinical trial of ibrutinib with rituximab (IR) in patients with relapsed/refractory mantle cell lymphoma (MCL). *British Journal of Haematology, 182*(3), 404-411. doi:10.1111/bjh.15411

Jain, P., & Wang, M. L. (2022). Mantle cell lymphoma in 2022 - A comprehensive update on molecular pathogenesis, risk stratification, clinical approach, and current and novel treatments. *American Journal of Hematology, 97*(5), 638-656. doi:10.1002/ajh.26523

Jain, P., Zhao, S., Lee, H. J., Hill, H. A., Ok, C. Y., Kanagal-Shamanna, R., … Wang, M. L. (2022). Ibrutinib with rituximab in first-line treatment of older patients with mantle cell lymphoma. *Journal of Clinical Oncology, 40*(2), 202-212. doi:10.1200/JCO.21.01797

Khouri, I. F., Saliba, R. M., Okoroji, G. J., Acholonu, S. A., & Champlin, R. E. (2003). Long-term follow-up of autologous stem cell transplantation in patients with diffuse mantle cell lymphoma in first disease remission. *Cancer, 98*(12), 2630-2635. doi:10.1002/cncr.11838

Kuo, P. Y., Jatiani, S. S., Rahman, A. H., Edwards, D., Jiang, Z., Ahr, K., … Ye, B. H. (2018). SOX11 augments BCR signaling to drive MCL-like tumor development. *Blood, 131*(20), 2247-2255. doi:10.1182/blood-2018-02-832535

Le Gouill, S., Thieblemont, C., Oberic, L., Moreau, A., Bouabdallah, K., Dartigeas, C., … Casasnovas, O. (2017). Rituximab after autologous stem-cell transplantation in mantle-cell lymphoma. *New England Journal of Medicine, 377*(13), 1250-1260. doi:10.1056/NEJMoa1701769

Lim S. Y., Horsman J. M. & Hancock B. W. (2010). The Mantle Cell Lymphoma International Prognostic Index: Does it work in routine practice? *Oncology Letters. 1*(1), 187-188. doi:10.3892/ol_00000034

Martin, P., Chadburn, A., Christos, P., Weil, K., Furman, R. R., Ruan, J., … Leonard, J. P. (2009). Outcome of deferred initial therapy in mantle-cell lymphoma. *Journal of Clinical Oncology, 27*(8), 1209-1213. doi:10.1200/JCO.2008.19.6121

MD Anderson Institutional Policy #CLN1202 - Advance Care Planning Policy. Advance Care Planning (ACP) Conversation Workflow (ATT1925)

National Comprehensive Cancer Network. (2024). *B-Cell Lymphomas* (NCCN Guideline V1.2024). Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf

Continued on next page

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SUGGESTED READINGS - continued

Ning, M. S., Pinnix, C. C., Chapman, B. V., Gunther, J. R., Milgrom, S. A, Khoury, J. D., … Dabaja, B. S. (2019). Low-dose radiation (4Gy) with/without concurrent chemotherapy is highly effective for relapsed, refractory mantle cell lymphoma. *Blood Advances, 3*(13), 2035-2039. doi:10.1182/bloodadvances.2019030858

Robak, T., Jin, J., Pylypenko, H., Verhoef, G., Siritanaratkul, N., Drach, J., … Okamoto, R. (2018). Frontline bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone (VR-CAP) versus rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in transplantation-ineligible patients with newly diagnosed mantle cell lymphoma: Final overall survival results of a randomised, open-label, phase 3 study. *The Lancet Oncology, 19*(11), 1449-1458. doi:0.1016/S1470-2045(18)30685-5

Romaguera, J. E., Fayad, L. E., Feng, L., Hartig, K., Weaver, P., Rodriguez, M. A., … Wang, M. (2010). Ten-year follow-up after intense chemoimmunotherapy with Rituximab-HyperCVAD alternating with Rituximab-high dose methotrexate/cytarabine (R-MA) and without stem cell transplantation in patients with untreated aggressive mantle cell lymphoma. *British Journal of Haematology, 150*(2), 200-208. doi:10.1111/j.1365-2141.2010.08228.x

Romancik, J. T., & Cohen, J. B. (2020). Is limited-stage mantle cell lymphoma curable and how is it best managed?. *Hematology/Oncology Clinics*, *34*(5), 849-859. doi:10.1016j.hoc.2020.06.003

Ruan, J., Martin, P., Shah, B., Schuster, S. J., Smith, S. M., Furman, R. R., … Katz, O. (2015). Lenalidomide plus rituximab as initial treatment for mantle-cell lymphoma. *New England Journal of Medicine, 373*(19), 1835-1844. doi:10.1056/NEJMoa1505237

Rummel, M. J., Al-Batran, S. E., Kim, S. Z., Welslau, M., Hecker, R., Kofahl-Krause, D., … Mitrou, P. S. (2005). Bendamustine plus rituximab is effective and has a favorable toxicity profile in the treatment of mantle cell and low-grade non-Hodgkin's lymphoma. *Journal of Clinical Oncology*, *23*(15), 3383-3389. doi:10.1200/JCO.2005.08.100

Rummel, M. J., Niederle, N., Maschmeyer, G., Banat, G. A., von Grünhagen, U., Losem, C., … Kaiser, U. (2013). Bendamustine plus rituximab versus CHOP plus rituximab as first-line treatment for patients with indolent and mantle-cell lymphomas: An open-label, multicentre, randomised, phase 3 non-inferiority trial. *The Lancet, 381*(9873), 1203-1210. doi:10.1016/S0140-6736(12)61763-2

Tam, C. S., Anderson, M. A., Pott, C., Agarwal, R., Handunnetti, S., Hicks, R. J., … Westerman, D. (2018). Ibrutinib plus venetoclax for the treatment of mantle-cell lymphoma. *New England Journal of Medicine, 378*(13), 1211-1223. doi:10.1056/NEJMoa1715519

Tessoulin, B., Chiron, D., Thieblemont, C., Oberic, L., Bouadballah, K., Gyan, E., … Le Gouill, S. (2021). Oxaliplatin before autologous transplantation in combination with high-dose cytarabine and rituximab provides longer disease control than cisplatin or carboplatin in patients with mantle-cell lymphoma: Results from the LyMA prospective trial. *Bone Marrow Transplantation, 56*(7), 1700–1709. doi:10.1038/s41409-020-01198-2

Thorsélius, M., Walsh, S., Eriksson, I., Thunberg, U., Johnson, A., Backlin, C., & Rosenquist, R. (2002). Somatic hypermutation and VH gene usage in mantle cell lymphoma. *European Journal of Haematology, 68*(4), 217-224. doi:10.1034/j.1600-0609.2002.01662.x

Wang, M., Fayad, L., Wagner-Bartak, N., Zhang, L., Hagemeister, F., Neelapu, S. S., … Cabanillas, F. (2012). Lenalidomide in combination with rituximab for patients with relapsed or refractory mantle-cell lymphoma: A phase 1/2 clinical trial. *The Lancet Oncology, 13*(7), 716-723. doi:10.1016/S1470-2045(12)70200-0

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SUGGESTED READINGS - continued

Wang, M., Jain, P., Lee, H. J., Ok, C. Y., Hill, H., Navsaria, L., … Flowers, C. R. (2021). Ibrutinib plus rituximab and venetoclax (IRV) followed by risk-stratified observation or short course r-hypercvad/MTX in young patients with previously untreated mantle cell lymphoma-Phase-II Window-2 clinical trial. *Blood*, *138*, 3525. doi:10.1182/blood-2021-153390

Wang, M. L., Jain, P., Zhao, S., Lee, H. J., Nastoupil, L., Fayad, L., … Wang, L. (2022). Ibrutinib-rituximab followed by R-HCVAD as frontline treatment for young patients (≤ 65 years) with mantle cell lymphoma (WINDOW-1): A single-arm, phase 2 trial. *The Lancet Oncology*, *23*(3), 406-415. doi:10.1016/S1470-2045(21)00638-0

Wang, M. L., Jurczak, W., Zinzani, P. L., Eyre, T. A., Cheah, C. Y., Ujjani, C. S., … Shah, N. N. (2023). Pirtobrutinib in covalent Bruton tyrosine kinase inhibitor pretreated mantle-cell lymphoma. *Journal of Clinical Oncology, 41*(24), 3988. doi:10.1200/JCO.23.00562

Wang, M., Munoz, J., Goy, A., Locke, F. L., Jacobson, C. A., Hill, B. T., … Reagan, P., M. (2020). KTE-X19 CAR T-cell therapy in relapsed or refractory mantle-cell lymphoma. *New England Journal of Medicine, 382*(14), 1331-1342. doi:10.1056/NEJMoa1914347

Wang, M., Munoz, J., Goy, A., Locke, F. L., Jacobson, C. A., Hill, B. T., … Reagan, P. M. (2023). Three-year follow-up of KTE-X19 in patients with relapsed/refractory mantle cell lymphoma, including high-risk subgroups, in the ZUMA-2 study. *Journal of Clinical Oncology, 41*(3), 555. doi:10.1200/JCO.21.02370

Wang, M. L., Rule, S., Martin, P., Goy, A., Auer, R., Kahl, B. S., … Blum, K. A. (2013). Targeting BTK with ibrutinib in relapsed or refractory mantle-cell lymphoma. *New England Journal of Medicine, 369*(6), 507-516. doi:10.1056/NEJMoa1306220

Wang, M., Rule, S., Zinzani, P. L., Goy, A., Casasnovas, O., Smith, S. D., … Panizo, C. (2018). Acalabrutinib in relapsed or refractory mantle cell lymphoma (ACE-LY-004): A single-arm, multicentre, phase 2 trial. *The Lancet, 391*(10121), 659-667. doi:10.1016/S0140-6736(17)33108-2

Xu, J., Wang, L., Li, J., Saksena, A., Wang, S. A., Shen, J., … Wang, M. (2019). SOX11-negative mantle cell lymphoma. *The American Journal of Surgical Pathology, 43*(5), 710-716. doi:10.1097/PAS.0000000000001233

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