PATHOLOGIC DIAGNOSIS

ESSENTIAL:
- Hematopathology review of all slides with at least one tumor paraffin block. Re-biopsy if consult material is non-diagnostic.
- Adequate immunophenotype to confirm diagnosis
  - Paraffin panel:
    - Pan B-cell marker (CD19, CD20, PAX5), CD3, CD5, CD10, and cyclin D1
    - Ki-67 (proliferation rate)
  - Flow cytometry immunophenotyping: kappa/lambda light chains, CD5, CD10, CD19, CD20, CD23, FMC-7, CD200 and CD43

OF USE IN CERTAIN CIRCUMSTANCES:
- Molecular genetic analysis
  - FISH to detect the t(11;14)(q13;q32)/CCND1-IgH
  - IgH gene rearrangements to detect monoclonality
  - PCR to detect CCND1-IgH
  - TP53 mutation
  - NOTCH1 mutation
- Immunohistochemistry for SOX-11

STRONGLY RECOMMENDED:
- Fine Needle Aspiration (FNA) or core biopsy for tissue banking by protocol

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
- B symptoms (fever, sweats, weight loss)
- CBC with differential, LDH, BUN, creatinine, albumin, AST, total bilirubin, alkaline phosphatase, serum calcium, uric acid
- Screening for HIV 1 and 2, hepatitis B and C (HbcAb, HbaAg, HCVAb)
- Beta-2 microglobulin
- Chest x-ray, PA and lateral
- Bone marrow bilateral biopsy with unilateral aspirate
- CT chest, abdomen and pelvis
- PET/CT
- Lifestyle risk assessment

OF USE IN SELECTED CASES:
- Upper GI/barium enema/endoscopy
- CT head or MRI brain
- Plain bone radiographs and bone scan
- Urine pregnancy test
- Discuss fertility preservation options and sperm banking for patients of child bearing potential
- Lumbar puncture
- Colonoscopy
- Stool guaiac
Mantle Cell Lymphoma

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

### INITIAL THERAPY

**PRESENTATION**

Un-treated Mantle Cell Lymphoma

- Age less than or equal to 65?
  - Yes
  - **MIPI** less than or equal to 3?
    - Yes
    - **Clinical trial**
      - R-HCVAD/R-MA
      - R-CHOP with **or** radiation therapy if early Stage I or II
      - R-Bendamustine **with** radiation therapy if early Stage I or II
      - Observation
      - Rituximab
      - R-CHOP/R-DHAP or R-HCVAD/R-MA followed by autologous stem cell transplant
    - No
      - **Clinical trial**
        - Modified R-HCVAD/R-MA
        - R-CHOP with **or** radiation therapy if early Stage I or II
        - R-Bendamustine with **or** without maintenance rituximab every 2 months
        - Radiation therapy if early Stage I or II
        - Observation
        - Rituximab
  - No
    - Yes
      - **Clinical trial**
        - R-HCVAD/R-MA
        - R-CHOP with **or** radiation therapy if early Stage I or II
        - R-Bendamustine with radiation therapy if early Stage I or II
        - R-CHOP/R-DHAP or R-HCVAD/R-MA followed by autologous stem cell transplant
      - No
        - **Clinical trial**
          - Modified R-HCVAD/R-MA
          - R-CHOP with **or** without maintenance rituximab every 2 months
          - Radiation therapy if early Stage I or II
          - Observation
          - Rituximab

**FOLLOW-UP**

- All the following as indicated below:
  - CBC with differential
  - Chemistry profile as clinically indicated
  - CT chest, abdomen and pelvis
  - Chest x-ray, PA and Lateral
  - PET/CT as clinically indicated
  - Unilateral bone marrow biopsy and aspirate
  - Lymphoma markers in bone marrow

- First year – every 3 months, then Years 2 and 3 – every 4 months, then Years 4 and 5 – every 6 months, then After year 5 – annually

---

1 MIPI = Mantle Cell International Prognostic Index, see Appendix A
2 Chemotherapy Abbreviations: R-HCVAD/R-MA: rituximab, cyclophosphamide, mesna, doxorubicin, and vincristine alternating with rituximab, methotrexate, and cytarabine. R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. R-DHAP: rituxinab and cisplatin, cytarabine and dexamethasone

Rev-rituximab: thalidomide, lenalidomide and rituximab

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Department of Clinical Effectiveness V5

Approved by the Executive Committee of the Medical Staff on 08/29/2017
Note: Consider Clinical Trials as treatment options for eligible patients.

**Mantle Cell Lymphoma**

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1. Clinical trial
2. R-HCVAD\(^1\) with or without R-MA
3. Bortezomib with or without rituximab
4. R-DHAP\(^1\)
5. Rituximab, gemcitabine and oxaliplatin
6. Rituximab with thalidomide
7. Rituximab with lenalidomide
8. Rituximab single agent
9. Ibritumomab (for patients with less than 20% bone marrow involvement)
10. Involved site radiotherapy
11. Bendamustine with rituximab
12. Single agent lenalidomide if bortezomib failure
13. R-ICE\(^1\)
14. Ibrutinib

**Chemotherapy Abbreviations:**
- R-HCVAD/ R-MA: rituximab cyclophosphamide, mesna, doxorubicin, and vincristine alternating with rituximab, methotrexate and cytarabine depending on clinical factors (e.g., age, bone marrow recovery)
- R-DHAP: rituximab, cisplatin, cytarabine and dexamethasone
- Rev-rituximab: thalidomide, lenalidomide and rituximab
- R-ICE: rituximab, ifosfamide, etoposide, and carboplatin

Relapsed or refractory mantle cell lymphoma

- Response?
  - Yes
    - Consider additional treatment or clinical trial (e.g., radiotherapy and/or supportive care)
  - No
    - Allogeneic stem cell transplant if eligible or Autologous stem cell transplant

Relapse?

- Yes
  - Monitor per stem cell transplant
- No
  - Therapy plus Donor Lymphocyte Infusion (DLI) if prior allogeneic transplant

1. Allogeneic stem cell transplant if eligible
2. Supportive care
3. Therapy plus Donor Lymphocyte Infusion (DLI) if prior allogeneic transplant

Monitor per stem cell transplant
APPENDIX A: Mantle Cell Lymphoma International Prognostic Index (MIPI)
(Used to stratify patients into risk groups according to the four prognostic factors)

<table>
<thead>
<tr>
<th>Points</th>
<th>Age</th>
<th>ECOG Performance Status</th>
<th>LDH (ULN)</th>
<th>WBC (10^9/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Less than 50</td>
<td>0 - 1</td>
<td>Less than 0.67</td>
<td>Less than 6.700</td>
</tr>
<tr>
<td>1</td>
<td>50 - 59</td>
<td>-</td>
<td>0.67 – 0.99</td>
<td>6.700 – 9.999</td>
</tr>
<tr>
<td>2</td>
<td>60 - 69</td>
<td>2 - 4</td>
<td>1.0 – 1.49</td>
<td>10.000 – 14.999</td>
</tr>
<tr>
<td>3</td>
<td>Greater than or equal to 70</td>
<td>-</td>
<td>Greater than or equal to 1.5</td>
<td>Greater than or equal to 15.000</td>
</tr>
</tbody>
</table>

Total point score:
0-3 low
4-5 intermediate
6-11 high risk
Mantle Cell Lymphoma

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SUGGESTED READINGS


NCCN Clinical Practice Guidelines in Oncology, Non-Hodgkin’s Lymphoma, NCCN V4.2014


Mantle Cell Lymphoma

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V5
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