Oncology Clinical Pathways
Marginal Zone Lymphoma
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Marginal Zone Lymphoma – Presumptive Conditions

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

Vietnam Veterans – Agent Orange Exposure or Specified Locations
• Non-Hodgkin’s lymphoma

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)
Marginal Zone Lymphoma – Nodal

**Supportive Care and Pre-Therapy Considerations** include Hepatitis B serologies prior to starting anti-CD20 antibody therapy (e.g. rituximab); consider HBV DNA if HBsAg or HBcAb positive; consider entecavir if HBsAg or HBcAb positive; COVID and pneumococcal vaccinations recommended; consider VZV/HSV and PJP prophylaxis with any bendamustine-regimen.

**Pathology Workup** includes sufficient flow cytometry or IHC workup to exclude other small B-cell lymphomas (e.g. CD5, CD10, CD103, CD200, CD11c, CD25, CD23, BCL2, BCL6, cyclin D1, Ki-67, etc.); some molecular testing may be diagnostically useful in certain circumstances.

**Stage** if clinically limited stage, perform bone marrow biopsy and PET/CT to confirm.

**Radiation** risk-benefit consideration should include assessment of side effect profile and goal of therapy (low dose of XRT, low side effects, expected very lengthy duration of response) together with consideration of life expectancy from non-lymphoma causes, as survival from limited stage marginal zone lymphoma is generally excellent.

**Indications for Therapy** local symptoms due to nodal disease, reduced organ function due to nodal disease, B-symptoms (fever, weight loss, night sweats), cytopenias (Hgb < 10 g/dL, platelets <100,000/mm3), or an increase in disease tempo.

Clinical Trial Resources https://clinicaltrials.gov/ and https://lls-forms.careboxhealth.com/?IRC=HCP

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Clinical trial(s) always considered on pathway.

**Marginal Zone Lymphoma - Nodal**

Hepatitis B or C status?

- Active Infection: Treat viral hepatitis
- No Active Infection: Stage? *

Stage?

- Stage I or contiguous Stage II: Refer to Radiation Oncology for consideration of radiation (24-30 Gy) *
- Not Stage I or contiguous Stage II: Indications for therapy? *

Indications for therapy?

- Yes: Bendamustine and rituximab (6 cycles)
- No: Monitor every 3-6 months

- Monitor every 3-6 months

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- Monitor every 3-6 months

- Monitor every 3-6 months

- Monitor every 3-6 months

- Monitor every 3-6 months

- Monitor every 3-6 months
Marginal Zone Lymphoma – Splenic

Supportive Care and Pre-Therapy Considerations include Hepatitis B serologies prior to starting anti-CD20 antibody therapy (e.g. rituximab); consider HBV DNA if HBsAg or HBeAb positive; consider entecavir if HBsAg or HBeAb positive; COVID and pneumococcal vaccinations recommended.

Pathology Workup includes sufficient flow cytometry or IHC workup to exclude other small B-cell lymphomas (e.g. CD5, CD10, CD103, CD200, CD11c, CD25, CD23, BCL2, BCL6, cyclin D1, Ki-67, etc.); some molecular testing may be diagnostically useful in certain circumstances.

Indications for Therapy include local symptoms related to splenomegaly or cytopenias due to hypersplenism or bone marrow involvement; autoimmune cytopenias should be treated with specific therapies for these situations.

Clinical Trial Resources [https://clinicaltrials.gov/](https://clinicaltrials.gov/) and [https://lls-forms.careboxhealth.com/?IRC=HCP](https://lls-forms.careboxhealth.com/?IRC=HCP)
Marginal Zone Lymphoma – Extranodal

Supportive Care and Pre-Therapy Considerations
- Hepatitis B serologies prior to starting anti-CD20 antibody therapy (e.g. rituximab);
- Consider HBV DNA if HBsAg or HBcAb positive;
- Consider entecavir if HBsAg or HBcAb positive;
- COVID and pneumococcal vaccinations recommended;
- Consider VZV/HSV and PJP prophylaxis with any bendamustine regimen.

Pathology Workup
- Includes sufficient flow cytometry or IHC workup to exclude other small B-cell lymphomas (e.g. CD5, CD10, CD103, CD200, CD11c, CD25, CD23, BCL2, BCL6, cyclin D1, KI-67, etc.);
- Some molecular testing may be diagnostically useful in certain circumstances;
- The presence of t(11;18) is associated with inferior response to H. pylori antibiotic therapy.

Indications for Therapy
- Cytopenias felt to be due to bone marrow involvement by lymphoma;
- Symptomatic adenopathy or splenomegaly, impaired organ function felt to be due to lymphoma.

Skin Directed Therapy
- Examples include palliative XRT, intralesional injection, topical steroids, topical imiquimod.

Stage
- If clinically limited stage, perform bone marrow biopsy and PET/CT to confirm.

Local Therapy
- In certain situations, surgery is used. Radiation risk-benefit consideration should include assessment of side effect profile and goal of therapy (low dose of XRT, low side effects, expected very lengthy duration of response) together with consideration of the expectancy from non-lymphoma causes as survival from limited stage marginal zone lymphoma is generally excellent; typically electronic beam radiation therapy.

Complete Lymphoma Response
- Assessment for response to H. pylori therapy for gastric MALT should include evaluation for clearance of H. pylori infection and evaluation for resolution of lymphoma (a complete response may take up to 18 months to be achieved);
- If there is persistent H. pylori infection, additional antibiotic therapy should be given; the presence of t(11;18) is associated with inferior response to H. pylori antibiotic therapy.

Clinical Monitoring
- Recommended after gastric MALT therapy and post-treatment endoscopy demonstrating complete response; routine endoscopy for asymptomatic patients is not recommended; the presence of t(11;18) may require closer monitoring.

Clinical Trial Resources
- https://clinicaltrials.gov/
- https://lls-forms.careboxhealth.com/?IRC=HCP

Clinical trial(s) always considered on pathway.
Marginal Zone Lymphoma – Relapsed or Refractory

Supportive Care and Pre-Therapy Considerations:
- Hepatitis B serologies prior to starting anti-CD20 antibody therapy (e.g., rituximab);
- Hepatitis C antiviral treatment if appropriate;
- Consider HBV DNA if Hep B seropositive; consider entecavir if Hep B seropositive;
- COVID and pneumococcal vaccinations recommended;
- Consider VZV/HSV and PJP prophylaxis with any bendamustine regimen.

Cross-Sectional Imaging:
- CT neck, chest, abdomen, and pelvis with IV contrast or FDG-PET/CT; PET/CT preferred if there is concern for transformation.

Biopsy:
- May include lymph node or any organ with appearance of involvement based on cross-sectional imaging; excisional biopsy is preferred; FNA is not appropriate.

Referral for Cellular Therapy (stem cell transplant, CAR T therapy) requires pre-transplant evaluation and review through TRACER.

Indications for Therapy:
- Local symptoms due to lymphoma, reduced organ function due to lymphoma, B-symptoms (fever, weight loss, night sweats), cytopenias (Hgb < 10 g/dL, platelets <100,000/mm3), or an increase in disease tempo.

Surveillance:
- Initially q3 months, then spaced to Q6-12 months, consisting of physical exam and labs; surveillance imaging is not recommended for asymptomatic patients.

Non-systemic Therapy Examples:
- Palliative XRT, intralesional injection, topical steroids, topical imiquimod and surgical resection.

Clinical Trial Resources:
- https://clinicaltrials.gov/
- https://lls-forms.carebohealth.com/?IRC=HCP

Clinical trial(s) always considered on pathway.

*Cross-sectional imaging CT neck, chest, abdomen, and pelvis with IV contrast or FDG-PET/CT; PET/CT preferred if there is concern for transformation.

*Indications for Therapy: local symptoms due to lymphoma, reduced organ function due to lymphoma, B-symptoms (fever, weight loss, night sweats), cytopenias (Hgb < 10 g/dL, platelets <100,000/mm3), or an increase in disease tempo.

*Surveillance: initially q3 months, then spaced to Q6-12 months, consisting of physical exam and labs; surveillance imaging is not recommended for asymptomatic patients.

*Non-systemic therapy: examples include palliative XRT, intralesional injection, topical steroids, topical imiquimod and surgical resection.