17 APRIL

Waldenström's macroglobulinemia
World Awareness Day

A SUMMARY OF

Waldenstrom's macroglobulinemia

An indolent lymphoma characterized by the presence of lymphoplasmacytic cells that secrete an excess of IgM protein; these are found in the bone marrow, spleen, lymph nodes, and liver among other sites.

Symptoms

Symptomatic anemia is the most common presentation of WM

Other symptoms:

Constitutional symptoms	Lymphadenopathy	Peripheral neuropathy	Bing-Neel syndrome	
Cold agglutinin disease	Splenomegaly	Cryoglobulinemia	Hyperviscosity	Amyloidosis

- Affects 3–4 people per million
- More common in men and in White people
- Average age at diagnosis is 70 years
- Exact cause unknown
- Possible link to autoimmune disorders
- Not directly inherited but can run in families

Diagnosis

Confirmatory diagnostic criteria of WM include presence the monoclonal IgM paraprotein and a lymphoplasmacytic infiltrate in the bone marrow

IgM presence can be detected using serum protein electrophoresis and immunofixation

Clonal infiltration of the bone marrow can be confirmed by positive expression of surface IgM, CD19, CD20, CD25, and CD27

A bone marrow aspirate should also be obtained to evaluate *MYD88* and *CXCR4* mutational status

Additional diagnostics include:

- Complete blood counts
- Comprehensive metabolic panel
- Immunoglobulins
- Serum viscosity
- β-2-microglobulin
- Cryoglobulins
- Cold agglutinins
- Baseline CT scans

Treatment

Criteria

Not all patients require treatment at diagnosis. Therapy initiation indicators include:

Development of symptomatic anemia with a hemoglobin ≤10 g/dL that is secondary to the WM*

Platelets <100,000 mm^3*	Symptomatic hyperviscosity	Symptomatic extramedullary disease*	Moderate to severe neuropathy*
Constitutional symptoms*	Cold agglutinemia	Cryoglobulinemia	Amyloidosis

When feasible, ***clinical trial enrollment*** should be considered for newly-diagnosed or R/R WM

*other possible causes ruled out

First-line

BTKis have become a mainstay of first-line therapy and is continued until disease progression or unacceptable toxicity

Bendamustine-rituximab is a common option with a finite duration of treatment (4–6 cycles)

Proteasome inhibitor-based regimens, such as rituximab-bortezomib-dexamethasone, are an option (with consideration for potential neuropathy)

BTKis for the treatment of WM:

- The FDA has approved both ibrutinib (± rituximab) and zanubrutinib.
- Side effects include risk of infection, bleeding, gastrointestinal symptoms, cytopenia, arthralgia or myalgia, AF.
- Recent data suggests newer BTKis, such as zanubrutinib, may provide the same efficacy with less off-target effects.

Relapsed/refractory

Any not previously used front-line treatment

A two-year course of venetoclax can be used

Life expectancy

Most patients will live for many years and potentially decades. The rIPSSWM can be used to define the risk group of a patient based on age, β-2-microglobulin, lactate dehydrogenase, and albumin. This tool estimates survival from the initiation of first-line chemoimmunotherapy. It is not validated for BTKi.

rIPSSWM

The revised International Prognostic Scoring System for WM

Patient resources

The International Waldenstrom's Macroglobulinemia Foundation (IWMF): **www.iwmf.com**

CancerCare: **www.cancercare.org**

Cancer Support Community (CSC): **www.CancerSupportCommunity.org**

Leukemia & Lymphoma Society (LLS): **www.lls.org**

Lymphoma Coalition (LC): **www.lymphomacoalition.com**

Lymphoma Research Foundation (LRF): **www.lymphoma.org**

AF, atrial fibrillation; BTKi, Bruton's tyrosine kinase inhibitor; CT, computerized tomography; FDA, Food and Drug Administration; IgM, immunoglobulin; R/R, relapsed/refractory; WM, Waldenstrom's macroglobulinemia.

LymphomaHub | IWMF | CELLECTAR BIOSCIENCES

The International Waldenstrom's Macroglobulinemia Foundation (IWMF) and the Lymphoma Hub are working in collaboration for patients with WM. This initiative aims to increase awareness of WM among healthcare professionals, patients, caregivers, and the patient advocacy community. This initiative is funded by Cellectar Biosciences. All content is developed independently by SES in collaboration with an expert steering committee; funders are allowed no direct influence on the content of the hub.

Sarosiek S and Castillo JJ. Talking with your Waldenström macroglobulinemia (WM) patients. IWMF. https://iwmf.com/wp-content/uploads/2022/10/IWMF-WM-guide_web.pdf. Published Sep 2022. Accessed March 01, 2023.