Defining your patient's treatment plan

Find out what your next steps should be in planning your patient's treatment

Indications for treatment initiation in patients with WM[1]

Clinical

These clinical symptoms are indications treatment should be initiated in your patient:

- Recurrent fever, night sweats, weight loss, fatigue
- Hyperviscosity
- Lymphadenopathy: either symptomatic or bulky (maximum diameter of at least 5 cm)
- Symptomatic hepatomegaly and/or splenomegaly
- Symptomatic organomegaly and/or organ or tissue infiltration
- Peripheral neuropathy due to WM

Laboratory

If your patient displays the following laboratory findings, treatment should be initiated:

- Symptomatic cryoglobulinaemia
- Symptomatic cold agglutinin anaemia
- Autoimmune haemolytic anaemia and/or thrombocytopaenia
- Nephropathy related to WM
- Amyloidosis related to WM
- Hb ≤10 g/dL
- Platelets <100x109/L
- IgM levels >60 g/L

The ESMO guidelines for the management of WM outline clinical and laboratory indications for treatment initiation.[1]

To treat or not to treat?

Patients with low Hb levels, high lymphoplasmacytic cell infiltration, IgM flare and high ß2-microglobulin levels may be at higher risk for development of symptomatic WM.[2,3]

However, patients may be asymptomatic for 5–10 years and can be managed with a 'watch and wait' approach, without treatment and should be followed up every 3–6 months.[1–3]

No data exist to support early initiation of therapy over a watch and wait strategy, nor is the level of monoclonal IgM alone an indication to start treatment.[1]

Hyperviscosity is a clinical emergency. Plasmapheresis should be used immediately in patients with symptomatic hyperviscosity, in addition to appropriate systemic therapy for WM.[1]

Additional tests

Additional workup is often based on symptomatic presentation and laboratory findings that can indicate the need for treatment initiation.[1]

Clinically-indicated diagnostic work-up[1]

Symptom / clinical presentation	Test
Hyperviscosity syndrome - headaches, visual disturbances, confusion, epistaxis	• Cryoglobulins • Cold agglutinine titre • Serum viscosity
Anaemia with haemolysis	• Coombs testing • Cold agglutinine titre
Raynaud-like symptoms, acrocyanosis, ulcerations of the extremities	• Cryoglobulins
Bleeding	• Screening for acquired von Willebrand disease
Neuropathy	• Myelin-associated glycoprotein (anti-MAGs) • Specialist neurologocal evaluation
Amyloidosis	• Fat aspirate stained with Congo red • Cardiac and renal biomarkers

Types of WM treatment

Watch and wait

For asymptomatic patients with acceptable IgM blood levels, no treatment is required. These patients will be monitored and seen by their clinic every 3–6 months for review.[4]

This course of action may seem confusing at first, but as there is no evidence that treating early in asymptomatic patients is beneficial, 'watch and wait' is applied in order to maintain the patient's quality of life.[4]

Treatment will begin if the patient:[4]
Develops WM-related symptoms
Has elevated levels of IgM protein in the blood or they experience hyperviscosity
Experiences changes in blood count (eg, anaemia)
Develops other complications (eg, progressive neuropathy, cryoglobulinaemia, or cold agglutinin disease)

Treating symptoms

Treatment may be required to treat WM symptoms and side effects of WM treatment, which include[5]:
Plasmapheresis, when a patient has high levels of IgM resulting in hyperviscosity
Blood transfusions or platelet transfusions to combat low blood or low platelet counts
Immunoglobulin replacement therapy, for patients with low antibody levels
Antibiotics or antiviral drugs, to prevent infections

Treating WM

There are a range of different treatment options for WM patients[4,6]:
Chemotherapy, given orally intravenously or subcutaneously
Steroids, often used in conjunction with chemotherapy
Monoclonal antibody therapy
Biological therapies
Stem cell transplantation
CAR T-cell therapy

Treatment selection should then be directed by the overall health of your patient, tumour burden, and clinical presentation.[1] Guideline therapy recommendations should be considered in conjunction with local practices and available treatment options.

Follow-up after WM treatment

Patients are monitored **every 3–6 months after finishing treatment**, possibly requiring further tests to assess their disease state. If they relapse from WM remission, depending on the response to their first-line treatment, this could be repeated, or they can be put in a second-line of treatment.[5]

CAR T-cell=chimeric antigen receptor T-cell; ESMO=European Society for Medical Oncology; IgM=immunoglobulin M; Hb=haemoglobin; WM=Waldenström's macroglobulinemia.

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