Treatment of Waldenström's Macroglobulinemia Mayo Consensus

Scottsdale, Arizona

Rochester, Minnesota

Jacksonville, Florida

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Mayo Clinic Consensus for Newly Diagnosed Waldenström's Macroglobulinemia

- Waldenstrom Macroglobulinemia (WM) is a B-cell lymphoproliferative disorder (LPD) characterized by lymphoplasmacytic infiltration of marrow and/or lymphatic tissue and monoclonal immunoglobulin M protein in the serum.
- For the diagnosis of smoldering WM, the Mayo Clinic criteria require marrow infiltration by ≥ 10% clonal lymphoplasmacytic cells and/or IgM monoclonal protein of ≥ 3g/dL and absence of end-organ damage/symptoms attributable to LPD.
- WM remains an incurable disease with the currently available therapies.
- Treatment is evolving rapidly as more effective agents and combinations become available.
- mSMART is a consensus opinion that takes into account the specific indications for treatment and the currently available therapeutic options.
- The general approach is presented here (mSMART – off-study). However, clinical trials must be considered and are preferred at every level.
- We recommend that all patients with newly diagnosed WM be seen at least once at a referral center with expertise in the management of this rare disease.

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mSMART for WM

- In cases of suspected lymphoplasmacytic lymphoma that are histopathologically difficult to interpret, we recommend checking MYD88 L265P mutation status by allele-specific polymerase-chain-reaction (AS-PCR) assay.
- In addition to performing a bone marrow (± lymph node/involved tissue) biopsy and monoclonal protein studies at diagnosis, we check CBC, liver function tests, creatinine, serum beta 2 microglobulin, lactate dehydrogenase, computerized tomography (CT) of chest, abdomen and pelvis or a combined 18F-FDG positron emission tomography (PET)/CT scan for assessment of lymphadenopathy, extramedullary disease /organomegaly.
- Cryocrit, serum viscosity, Coombs test /cold autoantibody, electromyogram and hepatitis C profile may be checked depending on the presenting signs/symptoms.
- If coexisting AL-Amyloidosis is suspected, NT-pro BNP, troponin T, echocardiogram with strain imaging, coagulation parameters and a fat aspirate to detect amyloid material should be performed.
- Fundoscopic examination is recommended in all patients with visual disturbance, hyperviscosity symptoms and/or IgM ≥3000 mg/dL.
- Clinicians should be aware of rituximab-induced IgM flare, the delay in achieving maximal response post-therapy as well as the discordance between the monoclonal protein and bone-marrow response states with certain therapies (e.g. ibrutinib, everolimus).

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Consensus for Newly Diagnosed Waldenström Macroglobulinemia

- IgM MGUS (<10% lymphoplasmacytic infiltration)
- Asymptomatic/smoldering Waldenstrom's
- Hemoglobin ≥11 g/dL
- Platelets ≥120 x 10^9/L

- Hemoglobin <11 g/dL or symptomatic
- Platelets <120 x 10^9/L
- IgM-related neuropathy
- WM-associated hemolytic anemia
- Symptomatic cryoglobulinemia

- Bulky Disease
- Profound cytopenias –
  - Hemoglobin ≤10 g/dL
  - Platelets <100 x10^9/L
- Constitutional symptoms
- Hyperviscosity symptoms

Hyperviscosity symptoms

Yes

No

Plasmapheresis

Observation

Single Agent Rituximab†

(1 cycle; no maintenance therapy)
†plasmapheresis if hyperviscosity develops with treatment

Bendamustine + Rituximab (BR)* x 4-6 cycles
No rituximab maintenance therapy

Harvest stem cells if ≤ 70 years and potential autologous stem cell transplantation candidate in future

*__Dexamethasone + Rituximab +Cyclophosphamide (DRC)__ x 6 cycles is an alternative if the disease burden is low

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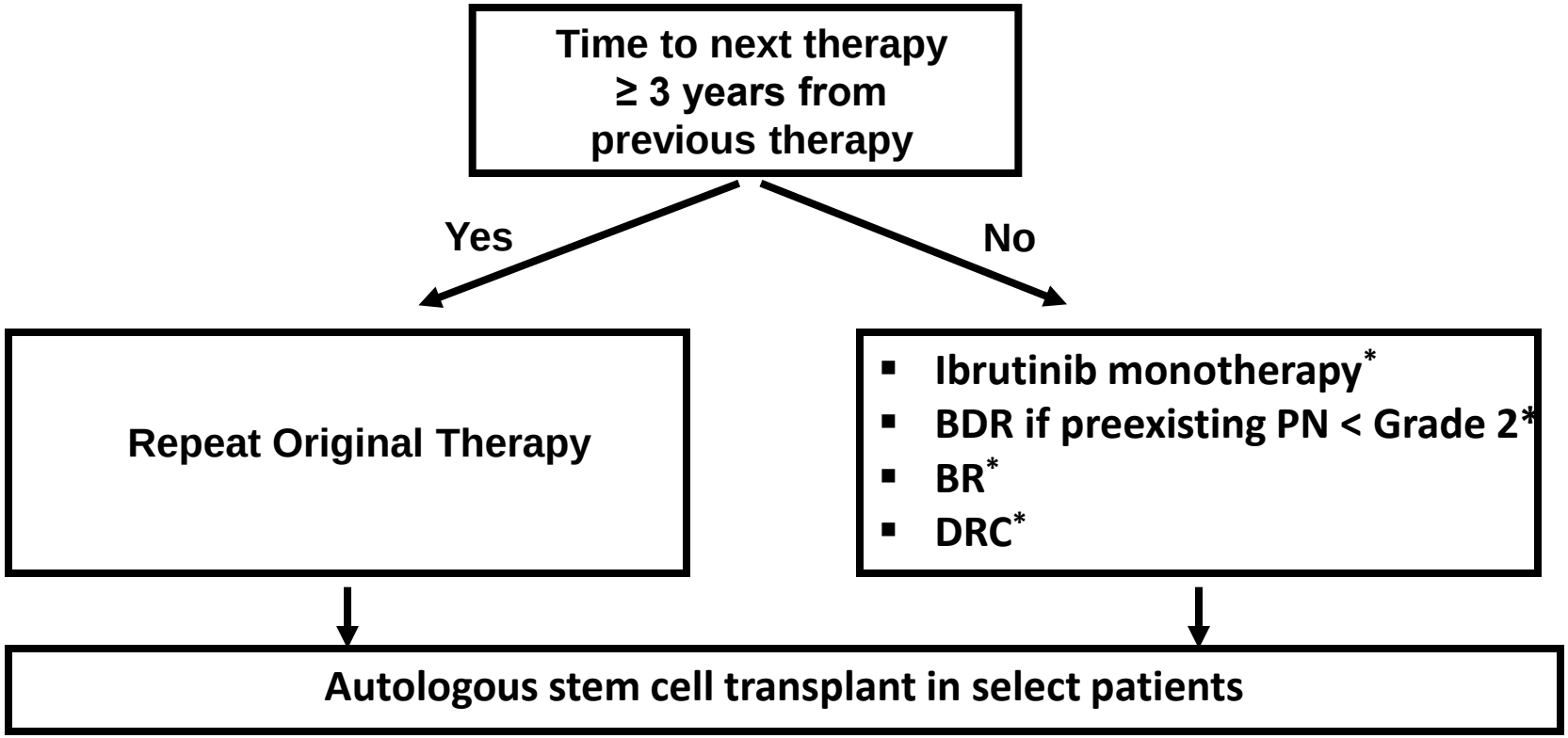
Waldenström Macroglobulinemia Consensus for Salvage Therapy



*If not previously used.

For multiply relapsed or refractory disease, in addition to the regimens listed above, consider nucleoside analog (cladribine or fludarabine)-based regimens or everolimus as alternatives.

DRC = Dexamethasone + Rituximab + Cyclophosphamide; BR = Bendamustine + Rituximab; BDR = Bortezomib (weekly), Dexamethasone + Rituximab; PN= peripheral neuropathy