Waldenström's macroglobulinemia

WHAT IS WALDENSTRÖM'S MACROGLOBULINEMIA?

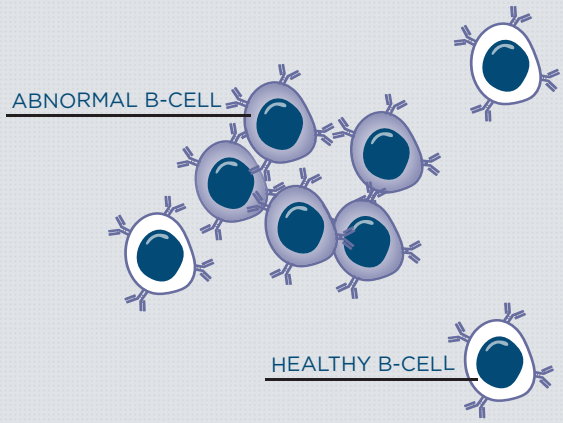
Waldenström's macroglobulinemia (WM) is a rare, incurable blood cancer, primarily found in the bone marrow.[1]

- WM is classified as **a form of non-Hodgkin's lymphoma,** representing about **1%** of all cases.[2]

- Common symptoms associated with WM are **weakness, loss of appetite, fever, sweats, weight loss, and neuropathy.** Less common symptoms are **enlarged lymph nodes, swollen abdomen, abnormal bleeding or heart problems.**[3]

- **WM is a slowly-progressing disease**, with an overall relative five-year survival rate of about **78%**.[2,4]

- **WM begins in B-cells, a type of white blood cell involved in immune system response.** As the disease progresses, WM can lead to an accumulation of proteins that interrupt normal blood cell development in the bone marrow, which may result in symptoms.[1]



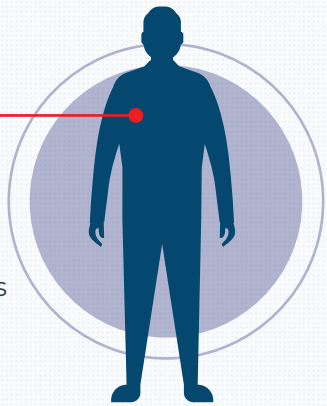
WHO DOES WM AFFECT?

- The incidence of WM is about **three cases per million** in the U.S.[5]

1,000 TO 1,500

people are diagnosed with WM each year in the U.S.[5]

- WM is **more common in men** than in women, and most often occurs in older adults – the average age at diagnosis is 70 years old.[5]



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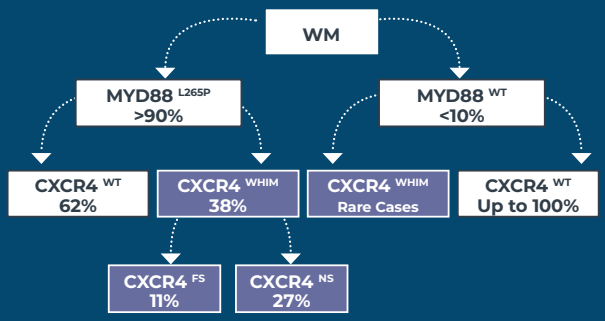
MUTATIONS IN WM[6,7]

- Though the exact causes of WM are still unknown, **research suggests that gene mutations may trigger changes in B-cells, which cause abnormal cells to multiply.**
  - **MYD88 mutations:** Up to **90%** of WM patients have an abnormal version of the MYD88 gene.
  - **CXCR4 mutations:** Approximately four out of 10 (**40%**) patients with WM have changes to the CXCR4 gene. Usually, CXCR4 mutations are found in patients with MYD88 mutations, though they can also be present in patients with MYD88 genes functioning normally (wild-type).

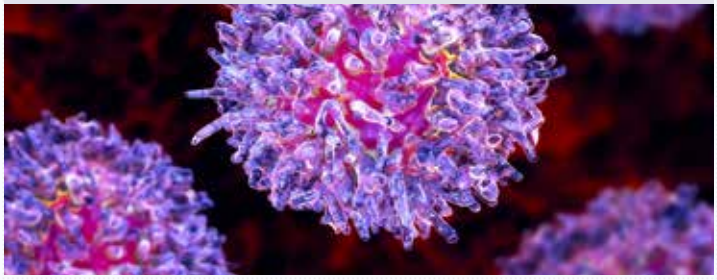


HOW IS WM DIAGNOSED AND TREATED?

- WM is often diagnosed when a patient sees their doctor about symptoms they are experiencing. Other times, it can present during routine blood tests. Several types of biopsies can also diagnose WM.[8]
- While there is no cure for WM, there are several treatment options available, which may vary for each patient based on stage of disease, age and overall health. Treatments include:
  - **Chemotherapy**
  - **Radiation**
  - **Stem cell transplants**
  - **Plasmapheresis**[9]
  - **Immunotherapies**[10]
    - Monoclonal antibodies, such as rituximab, attach to cancer cells and trigger cell death
  - **Targeted therapies**[11]
    - Proteasome inhibitors, such as bortezomib, block proteins responsible for cell growth and survival
    - BTK inhibitors block proteins that tell abnormal cells to grow

IMPACT OF MUTATIONS ON DISEASE PROGRESSION

- **MYD88** and **CXCR4** mutations can have an impact on disease progression and the efficacy of some targeted therapies.[6,7]
  - **In clinical trials, patients with** MYD88 mutations and CXCR4 wild-type gene expression had better outcomes and deeper responses with certain treatments.[7]
  - **Patients with wild-type MYD88** tend to experience worse outcomes and lower overall survival, and may have a delayed response to treatment.[7]
  - **CXCR4 mutations** can be associated with a more aggressive disease and show resistance or delayed response to treatment.[6,7]



WM can be a devastating disease for patients and their families. Early diagnosis and awareness is key to improved outcomes.

[1] American Cancer Society. What Is Waldenstrom Macroglobulinemia? Accessed February 2021. Available at https://www.cancer.org/cancer/waldenstrom-macroglobulinemia/about/what-is-wm.html/.
[2] Lymphoma Research Foundation. Understanding Waldenstrom Macroglobulinemia Lymphoma. Accessed February 2021. Available at https://lymphoma.org/wp-content/uploads/2020/09/LRF_Factsheet_Waldenstro%CC%88m-Macroglobulinemia_090920.pdf.
[3] American Cancer Society. Signs and Symptoms of Waldenstrom Macroglobulinemia. Accessed February 2021. Available at https://www.cancer.org/cancer/waldenstrom-macroglobulinemia/detection-diagnosis-staging/signs-symptoms.html.
[4] American Cancer Society. Survival Rates for Waldenstrom Macroglobulinemia. Accessed February 2021. Available at https://www.cancer.org/cancer/waldenstrom-macroglobulinemia/detection-diagnosis-staging/survival-rates.html.
[5] American Cancer Society. Key Statistics About Waldenstrom Macroglobulinemia. Accessed February 2021. Available at https://www.cancer.org/cancer/waldenstrom-macroglobulinemia/about/key-statistics.html.
[6] Kaiser, et al. CXCR4 in Waldenström's Macroglobulinemia: chances and challenges. *Leukemia.* December 2020. 35:333–345.
[7] Treon, et al. Genomic Landscape of Waldenström Macroglobulinemia and Its Impact on Treatment Strategies. *Journal of Clinical Oncology.* February 2020. 38:1198-1208.
[8] American Cancer Society. Tests for Waldenstrom Macroglobulinemia. Accessed February 2021. Available at https://www.cancer.org/cancer/waldenstrom-macroglobulinemia/detection-diagnosis-staging/how-diagnosed.html.
[9] American Cancer Society. Treating Waldenstrom Macroglobulinemia. Accessed February 2021. Available at https://www.cancer.org/cancer/waldenstrom-macroglobulinemia/treating.html.
[10] American Cancer Society. Biological Therapy or Immunotherapy for Waldenstrom Macroglobulinemia. Accessed February 2021. Available at https://www.cancer.org/cancer/waldenstrom-macroglobulinemia/treating/biologicaltherapy-immunotherapy.html.
[11] American Cancer Society. Targeted Drugs for Waldenstrom Macroglobulinemia. Accessed February 2021. Available at https://www.cancer.org/cancer/waldenstrom-macroglobulinemia/treating/targeted-therapy.html.

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