Dana-Farber Cancer Institute | The Jimmy Fund®

2024 PROGRESS UPDATE

International Waldenstrom's Macroglobulinemia Foundation

Jorge Castillo, MD, Clinical Director, Bing Center for Waldenström's Macroglobulinemia

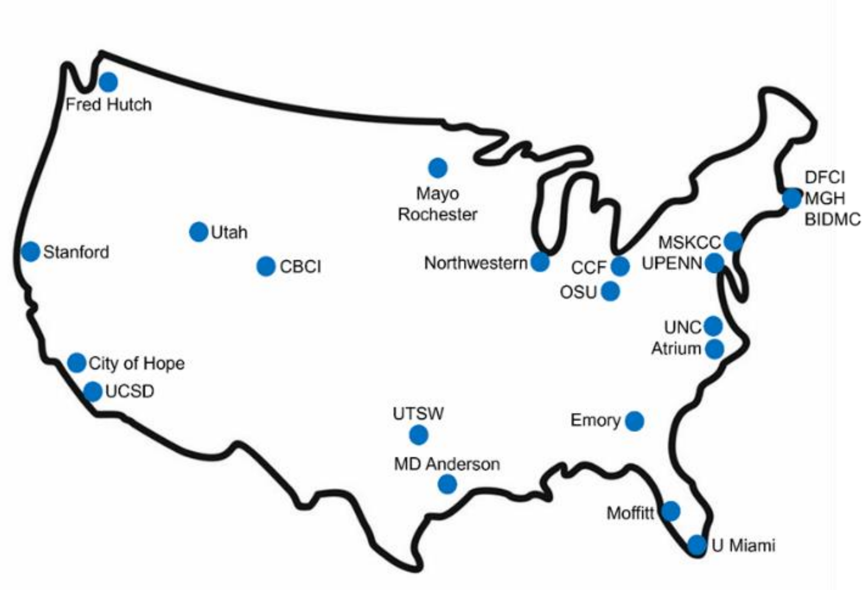
Steven Treon, MD, PhD, Director, Bing Center for Waldenström's Macroglobulinemia

Introduction

WM-NET, a multi-institutional network established in October 2023 and spearheaded by **Jorge Castillo, MD,** and **Steven Treon, MD, PhD,** is dedicated to advancing clinical and research programs for Waldenström's macroglobulinemia (WM). The network's pioneering approach, which is centered on optimizing clinical trial design and accelerating the translation of research findings into practice, is rooted in a deep commitment to collaboration and innovation. During its inaugural year, WM-NET has made significant strides in hiring staff, launching clinical trials, and developing an infrastructure that will include a comprehensive database to drive future breakthroughs. This remarkable progress has been made possible thanks to the generous support of the International Waldenstrom's Macroglobulinemia Foundation, and we are grateful for your continued partnership in our work.

ASSEMBLING A ROBUST TEAM TO DRIVE PROGRESS

WM-NET now has a fully staffed, dedicated team in place to support its mission of advancing WM clinical research. **Lorraine Martinez** has been instrumental in her administrative role, facilitating the planning and organization of the WM-NET group meetings, which occur regularly throughout the year. As the clinical research coordinator, **Nina Budano** ensures the smooth operation and coordination of clinical trial efforts across the network. Most recently, in October 2024, **Courtney Boyajian** was hired as the research project manager, bringing fresh energy and expertise to the network. Additionally, WM-NET has expanded to 22 participating institutions across the country, while both U.S. and international WM specialists continue to serve as advisors. This robust staff and advisory board will play a crucial role in driving the network's initiatives forward.



Loncastuximab tesirine is not yet approved by the Food and Drug Administration (FDA) for WM, but it has been approved for other uses. **Antibody-drug conjugates** are therapies that are designed to deliver drugs directly to cancer cells by attaching them to antibodies that bind to proteins on the surface of cancer cells. This targeted strategy can increase specificity and limit toxicity.

Overall response rate refers to the percentage of people in a study or treatment group who have a partial or complete response to a treatment within a certain period of time. Overall response rate is one way to determine how well a treatment works.

LAUNCHING WM-NET'S FIRST CLINICAL TRIAL

WM-NET is actively working on several clinical trials to address patient needs. In one notable achievement, in 2024, the network launched its first clinical trial—a multicenter phase II trial of loncastuximab tesirine, an **antibody-drug conjugate** (see sidebar) for previously treated WM. Led by **Shayna Sarosiek, MD,** in collaboration with researchers from Mayo Clinic and Fred Hutchinson Cancer Research Center, this trial aims to test a new third-line treatment regimen for patients whose disease has progressed after first- and second-line treatments, including chemotherapy, immunotherapy, and targeted BTK inhibitors.

To date, seven patients have been enrolled, with an 86% **overall response rate** (see sidebar). The median time to a minor response was 14 days, and the time to a partial response or better was 60 days. Side effects have been mild to moderate, and none have led to treatment discontinuation. These early results are promising compared to other third-line treatments, especially for patients with high rates of CXCR4 and TP53 mutations. Looking ahead, the study team aims to enroll up to 36 patients to further validate these findings.

ADDITIONAL CLINICAL TRIALS LAUNCHING THIS YEAR

WM-NET is initiating two more clinical trials this year. One trial, spearheaded by Gottfried von Keudell, MD, at Beth Israel Deaconess Medical Center, with collaborators from the University of Texas Southwestern Medical Center and the University of North Carolina, is now enrolling participants on a trial to test epcoritamab in patients with previously treated WM. The second trial, led by Andrew Branagan MD, PhD, at Massachusetts General Hospital, is investigating the combination of zanubrutinib, bendamustine, and rituximab for treatment-naïve WM. This trial has obtained Institutional Review Board approval and is expected to begin accruing patients before the end of 2024. Alongside these efforts, WM-NET researchers are also currently writing other trial protocols.

Pictured: The WM-NET Inaugural Meeting in October 2023.

ESTABLISHING A CLINICAL DATABASE

In additional to its clinical trial efforts, WM-NET is focused on establishing a comprehensive database to support WM research. Research fellow **Alberto Guijosa, MD**, is creating a retrospective database for Dana-Farber, which will also be utilized by WM-NET. Under Castillo's guidance, this fellowship position offers valuable research and clinical experience to medical graduates, with the primary goal of building and maintaining a robust database that will eventually include prospective data from all WM-NET clinical trials.

These initiatives aim to fill existing gaps in WM research infrastructure and enhance the network's ability to conduct scientifically driven studies. By providing a centralized resource for data, the database will facilitate more comprehensive and collaborative research efforts, enabling scientists to uncover new insights into the disease's mechanisms and potential treatment targets. Ultimately, these efforts will accelerate the development of innovative therapies and improve outcomes for patients.

Pictured (left to right): Steve Treon, MD, PhD; Newton Guerin, IWMF President and CEO; Tom Hoffman, MD, IWMF Vice Chair, Research; Jorge Castillo, MD

The Impact of Your Philanthropy

The International Waldenstrom's Macroglobulinemia Foundation's support has been instrumental in driving WM-NET's remarkable advancements in its inaugural year. Thanks to your generosity, the network has successfully launched its first clinical trial, expanded staff and participating institutions, and laid the groundwork for a comprehensive database and biorepository. These efforts are not only advancing clinical research for WM but also paving the way for future breakthroughs that will improve patient care and outcomes. We are deeply grateful for your partnership in our efforts to transform the treatment landscape and make a meaningful impact in the lives of all those affected by WM.

Report prepared by Jodi Hyer.

450 Brookline Avenue, Boston, MA 02215 | dana-farber.org

10% of all designated gifts will support our Faculty Research Fund to advance Dana-Farber’s research mission.