



• CHRONIC LYMPHOCYtic LEUKEMIA •

CLL RESEARCH

2021 Year In Review

CLL Global has provided over \$32 million in research funding (2005-2021)

Greetings!

As I reflect on the past year, I am once again reminded of how extraordinary the CLL community is. When faced with a pandemic that disrupted almost every aspect of life, the community adapted in real time to understand and address the needs of CLL patients. For CLL Global, this included funding research into the effectiveness of COVID-19 vaccines in patients with CLL, research that has now expanded to include determining what additional level of protection vaccine boosters may provide. To ensure patients and their loved ones received factual, up to date information on navigating the COVID-19 pandemic, we hosted a virtual town hall where our expert panel provided practical, evidence-based information and answered questions from the audience. Throughout this unprecedented period, CLL Global has remained committed to accelerating discoveries that promise the delivery of increasingly effective treatment options. Thank you for partnering with us to create a future that is free from the threat of CLL.



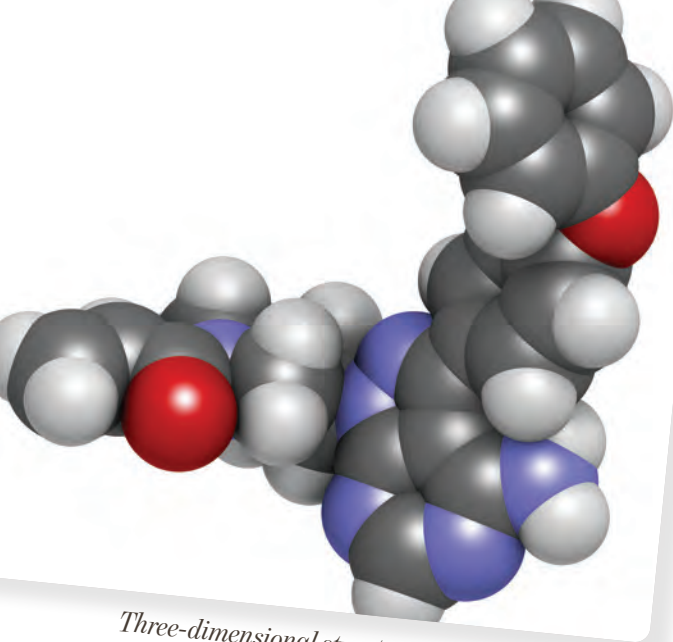
Congratulations, Dr. Wierda!

Initial results from the phase 2 CAPTIVATE trial have just been published online in the *Journal of Clinical Oncology*. The study evaluated minimal residual disease (MRD)-guided treatment discontinuation in patients <70 years old with previously untreated CLL who received 3 months of ibrutinib followed by 12 cycles of ibrutinib plus venetoclax. High rates of undetectable MRD (uMRD) were observed following treatment discontinuation and the 30-month progression-free survival rate was 95%. "The ibrutinib plus venetoclax combination for first-line treatment of patients with CLL or SLL represents an all-oral, once-daily, chemotherapy-free regimen that provides high rates of uMRD," wrote lead investigator, William Wierda, MD, PhD, D.B. Lane Cancer Research Distinguished Professor at the University of Texas MD Anderson Cancer Center. This limited-duration treatment is expected to be approved by the U.S. Food & Drug Administration in the coming months.

► [J Clin Oncol. 2021 Oct 7;JCO2100807. doi: 10.1200/JCO.21.00807. Online ahead of print.](https://doi.org/10.1200/JCO.21.00807)

Ibrutinib Plus Venetoclax for First-Line Treatment of Chronic Lymphocytic Leukemia: Primary Analysis Results From the Minimal Residual Disease Cohort of the Randomized Phase II CAPTIVATE Study

William G Wierda¹, John N Allan², Tanya Siddiqi³, Thomas J Kipps⁴, Stephen Opat⁵, Alessandra Tedeschi⁶, Xavier C Badoux⁷, Bryone J Kuss⁸, Sharon Jackson⁹, Carol Moreno¹⁰, Ryan Jacobs¹¹, John M Pagel¹², Ian Flinn¹³, Yvonne Pak¹⁴, Cathy Zhou¹⁴, Edith Szafer-Glusman¹⁴, Joi Ninomoto¹⁴, James P Dean¹⁴, Danelle F James¹⁴, Paolo Ghia¹⁵, Constantine S Tam¹⁶



Three-dimensional structure of ibrutinib.

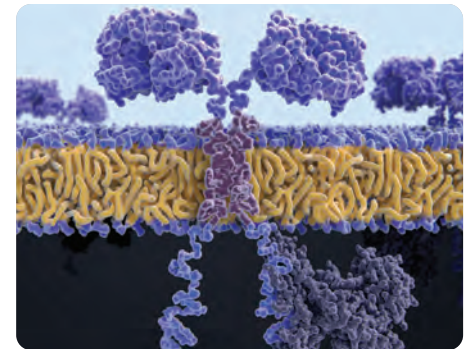
Notable Clinical TRIAL UPDATES

Fixed-duration ibrutinib and venetoclax is also effective when used in a population of older CLL patients (>65 years old). In a late breaking abstract presented at the 2021 European Hematology Association meeting, results of the phase 3 GLOW study showed that ibrutinib plus venetoclax achieved significantly longer progression-free survival (PFS) and a nearly 80% reduction in risk of progression or death compared with chlorambucil plus obinutuzumab.

After a median follow-up of 27.7 months, “the median PFS was 21 months for the combination of chlorambucil and obinutuzumab but has not yet been reached in the group randomized to ibrutinib plus venetoclax,” reported Arnon Kater, MD, PhD, deputy head of the Department of Hematology at Amsterdam Medical Center.

CELLULAR THERAPY FOR CLL

Updated findings from the phase 1 TRANSCEND CLL 004 trial investigating CAR-T cell therapy (liso-cel) alone or in combination with ibrutinib in heavily-pretreated, high risk patients were recently presented at the 2021 International Workshop on CLL. The combination of liso-cel and ibrutinib elicited a complete response rate of 59%, with 86% of patients achieving uMRD. “The combination elicited significant activity in this high-risk patient population and potentially predicts for earlier integration of CD19-directed CAR T-cell therapies into the treatment armamentarium of patients with CLL” said lead author Dr. William Wierda.



*Chimeric Antigen Receptor (CAR)
T-cell illustration.*

HIGHLIGHTING OUR RESEARCH PARTNERS: DR. CATHERINE WU



*Dr. Catherine Wu,
Professor, Dana-Farber
Cancer Institute &
Harvard Medical School.*

It is our pleasure to introduce you to our most recent grant recipient, Dr. Catherine Wu, Professor, Dana-Farber Cancer Institute and Harvard Medical School. Dr. Wu’s research focuses on how to effectively mount an immune response to recognize and eradicate cancer.

How did you become interested in CLL research?

I have been long fascinated by trying to address the question of why there is so much clinical variability in the disease course of patients with CLL. Why do some patients have a very indolent course? Why do some have a very aggressively paced course? This compounded by complex interplay between the CLL cells and the host immune response that we know is present in patients with CLL has drawn me to this disease.



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What aspects of CLL are you currently focused on in your laboratory?

We are deeply interested in understanding the basis for the molecular heterogeneity of the disease and also integrating this information to devise novel therapies to eradicate CLL. This has led us to focus on the use of genomics to comprehensively profile CLL. In turn, we have generated novel mouse models of disease that are highly reflective of human genetics so that we can mechanistically understand the impact of the molecular alterations that define CLL. Finally, we are dedicated to using genomics-guided approaches to generate personalized cancer vaccines for the treatment of CLL.

How is funding from CLL Global helping you? What question(s) are you trying to answer?

We are currently focused on dissecting the basis of immune dysfunction in CLL. This proposal aims to leverage single cell transcriptome data to identify novel interactions between CLL cells and immune cells contributing to immune dysfunction and to validate findings from our scRNAseq analysis. Finally, we will perform functional studies to better understand how we may develop strategies to enhance immune function in CLL.

How will your research benefit CLL patients?

Understanding the mechanisms leading to this dysfunction is vitally important, since these defects in immunity render patients more at risk of infections and at increased risk of secondary cancers and other complications. This immune dysfunction may contribute to lower rates of effectiveness of current forms of immunotherapy such as bone marrow transplantation and chimeric antigen receptor T-cell therapy.

When you are not working in the lab how do you spend your time?

I love spending time with my three teenagers. I love music, performing and performance, and I enjoy hiking with my husband. Oh yes—and I love good food and conversation.



Save the Date

CLL Global Town Hall

On July 29, 2021, over 170 people joined us for our inaugural CLL Global Virtual Town Hall. Based on overwhelmingly positive reviews, a second Virtual Town Hall has been scheduled for **Thursday, January 13, 2022, from 3:30 – 4:30 PM CT**. Join us to hear the latest CLL news presented at the American Society of Hematology Meeting being held December 11-14, 2021, learn about survivorship issues specific to patients with CLL, and get your questions answered by our experts. Registration is free, just visit our website at cllglobal.org and click on Upcoming Events to sign up.

Happy New Year!

“Never a holiday morning, never an old year ends, but someone thinks of someone; old days, old times, old friends.”

-Anonymous



We wish you the best in the coming year.

HOME FOR THE HOLIDAYS



With the holiday season in full swing, many people are looking forward to gathering with friends and family to celebrate. Aside from masking, hand washing and distancing, what precautions can CLL patients take to celebrate safely? As soon as you are able, get a COVID-19 vaccine booster. Evidence indicates that boosters can induce antibody production in many patients, even those who did not produce antibodies after their initial vaccination.

You may also consider getting yourself and those you will be around tested in the days prior to getting together. And if you do have any COVID-19 symptoms get tested right away. Monoclonal antibody therapy (casirivimab and imdevimab), which can limit the duration and severity of the illness, is most effective when given early in an infection. We wish everyone a safe and joyful season.

A NEW ERA IN CLL THERAPY

Thanks to remarkable therapeutic advances that have occurred over the last decade, an ever-increasing number of CLL patients are achieving durable, lasting responses to therapy. The momentum created by these innovations continues to drive the field forward, bringing with it emerging options for limited-duration treatment and new strategies for managing high-risk, relapsed or refractory patients. Despite this progress there remains essential work to be done. Restoring patients' immune function, managing Richter's Transformation, overcoming drug resistance, and preventing second cancers are just a few of the unmet needs in CLL, and this is where CLL Global will direct its focus in the new year. We remain deeply grateful to our donors, without whom this essential research would be impossible.



Did you know that you can support CLL Global while shopping online? Just go to the AmazonSmile website (<https://smile.amazon.com>), select CLL Global Research Foundation as your beneficiary, and the AmazonSmile Foundation will donate 0.5% of all eligible purchases to CLL Global.



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Our mission is to abolish CLL as a threat to the life and health of patients by accelerating CLL research.

Please consider making a donation today and help us turn our passion for finding a cure for CLL into a reality for patients around the world. To donate online, visit our website at cllglobal.org/donate. Donations may also be mailed to CLL Global Research Foundation, P.O. Box 301402, Unit 428, Houston, Texas 77230.