



• CHRONIC LYMPHOCYTIC LEUKEMIA •

# CLL RESEARCH

## 2020 Year In Review

*CLL Global has provided over \$30.1 million in research funding (2005-2020)*

## Greetings!

As we come to the close of 2020, a challenging year by anyone's definition, we are heartened by the accomplishments CLL Global has been able to achieve in spite of many obstacles. With the onset of the COVID-19 pandemic in the spring, life as we knew it forever changed. What did not change was our dedication to supporting innovative CLL research and the best and brightest trainees who will become the next generation of CLL super heroes. In spite of laboratories around the world being closed, some for months at a time, and clinics reducing in-person visits to protect patients and save limited resources, CLL Global stayed true to our mission and ended the year having awarded more funding for CLL research and clinical trials than ever before! In the words of our founder and friend, Dr. Michael Keating, "we are not done yet" and we remain focused on and committed to finding a cure for CLL. Speaking of Dr. Keating, he has a few thoughts he'd like to share.



## CLL – The New Era

G'day mates! I am once again reaching out to you from my home office as access to the hospital remains restricted. While I dearly miss seeing my friends at work, no doubt like many of you, I am learning to make the most of my new-found free time. Brainstorming ideas with colleagues over FaceTime is not quite the same as in person over a cup of coffee, but it is still effective at stimulating my thought processes. These discussions have led me to conclude we are in a new era of CLL. Thanks to the remarkable advances in treatment that have occurred over the last 15 years, many of which CLL Global played a role in supporting, the majority of CLL patients today are living with low to no detectable minimal residual disease (MRD) and will remain that way for years and even decades. But as many of you know from personal experience that is far from the end of the story. There are still unmet needs in CLL, and my focus going forward will be to address them.

We need to understand, and in doing so, overcome drivers of resistance that can develop with small molecule inhibitors like ibrutinib and venetoclax. As the small molecule inhibitor landscape continues to grow, there is a need to prioritize what treatments are most appropriate for which patients at what time point. We must address the immune dysfunction that exists in CLL patients, which can lead to increased rates of infections and second cancers. We need strategies to identify those patients most at risk of developing Richter's transformation and effective treatment options for those who do. And most importantly we need to find a cure. Looking at our accomplishments over the last decade I am confident the next one will prove even more fruitful. Together, there is no stopping us!

*"So much of my life has revolved around my CLL friends and my patients. I care for and love y'all more than you know."*  
—Michael Keating



*Dr. Constantine Tam, M.B., B.S., M.D. from the Peter MacCallum Cancer Centre in Melbourne, Australia*

# FROM DOLLARS TO DISCOVERIES

CLL Global runs a tight ship with >90% of all donations going directly to fund leading-edge science. From basic and translational research to clinical trials, our grantees are committed to making a difference in the lives of CLL patients. Keep reading to learn how two of our current grant holders are turning dollars into discoveries.

"Thanks to the support of the CLL Global Research Foundation, our research group is able to pursue research into improving the lives of patients on modern therapies for CLL – how to manage side-effects such as bleeding and atrial fibrillation, figuring out how CLL cells develop resistance to our newest treatments, and testing the best combinations in the clinic. These issues which directly impact on patients' quality of life are often regarded as lower priority at many scientific research agencies, so we are extremely grateful to the CLL community who are continuing to support the research that leads to immediate improvements in the patients' lives."

"Funding from CLL Global Research Foundation has been instrumental for my laboratory to develop high risk/high-gain projects that are aimed at extending the lifespan of CLL patients. We look for very small ribonucleic acids, called microRNAs, in the plasma of patients in order to identify which patients will, in addition to CLL, develop other secondary cancers that are more aggressive and with a worse impact on survival than CLL. In many cases the DNA genes from the genome looks normal but the transcripts, i.e. microRNAs that are derived from the genes, are not normal. Funding from CLL Global Research Foundation has made possible my laboratory's discovery of these novel "microRNA mutations", a new and elusive category of alterations that can explain why some patients are not responding to the most advanced therapeutics. My partnership with CLL Global has kept alive this truly innovative research that is helping not only scientists and clinicians, but most importantly the patients who will benefit from better diagnostics and therapies."



*George Calin, M.D.,  
Ph.D. from The  
University of Texas MD  
Anderson Cancer Center*



*Varsha Gandhi, Ph.D.  
from The University of  
Texas MD Anderson  
Cancer Center*

Investigations that utilize RNA and protein sequencing technology provide valuable information that adds a new dimension to clinical and genetic knowledge of a disease such as CLL. In most cases, scientists focus on previously untreated patients with CLL to do such these "omics" evaluations. That is also preferred by granting agencies. We postulated that understanding and comparing the transcriptome (RNA) and proteome (protein) in CLL disease is not only needed for previously untreated CLL patients but also for those have received prior therapy. In fact this is an unmet need to identify the omics landscape of relapsed/refractory CLL disease. Such knowledge is critical for identification of druggable targets in CLL cells and precision medicine for these patients. That is our focus and we are grateful for the support that we have received from CLL Global to pursue these investigations.



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# THEY WORK!

There is excellent news on the COVID-19 vaccine front. On November 20, the drug maker Pfizer submitted an application to the Food and Drug Administration (FDA) for emergency use authorization for its vaccine. In a phase III clinical trial, the vaccine was found to be safe and 95% effective. It was also shown to work well in older people, an especially vulnerable population, and to prevent severe COVID-19. On November 30, the drug maker Moderna became the second vaccine developer to apply for emergency use authorization. Data from their clinical trial showed the vaccine is 94.1% effective at preventing coronavirus infections and 100% effective at preventing severe disease. It is quite possible both vaccines will be available for distribution to frontline workers before the end of the year.

The Pfizer and Moderna vaccines use a novel, RNA-based technology. Neither candidate is a “live” vaccine and should be safe for CLL patients. There are still important questions that need to be addressed including how long the protective effects of the vaccines last, whether they can prevent transmission of the virus, and whether the vaccines will work in high-risk groups including cancer patients. It is not time to let our guard down yet, but there is light at the end of the tunnel. Scientists are greeting these results with cautious enthusiasm and are optimistic the New Year will bring even more positive news on the vaccine front.



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## GOOD NEWS FROM 2020

This year the Food and Drug Administration (FDA) approved the combination of ibrutinib (I) and rituximab (R) for the frontline treatment of CLL. The approval was based on results from the phase 3 E1912 trial showing significantly improved progression-free survival among patients who received I+R compared to those who received fludarabine, cyclophosphamide, and rituximab (FCR).

Presenting at this year’s American Society of Hematology Meeting, being held virtually December 5-8, 2020, our very own Dr. William Wierda will report on data from the phase 2 CAPTIVATE study assessing fixed duration therapy of ibrutinib (I) plus venetoclax (Ven) in patients with treatment-naïve CLL. Treatment with I+Ven for 12 months produced high rates of undetectable minimal residual disease (uMRD) in both peripheral blood and bone marrow. Patients achieving uMRD were randomized into two groups, one receiving a placebo and the second continuing on I.

After 12 months the disease-free progression rate in patients randomized to placebo was similar to that of patients continuing on I, supporting a fixed-duration treatment-free remission in patients with CLL. In the relapsed/refractory setting, long term data from the phase 3 MURANO trial evaluating venetoclax plus rituximab (VenR) compared with bendamustine plus rituximab (BR) indicated that VenR produced a sustained progression-free survival benefit as compared to BR, particularly in patients with uMRD. Early use of VenR in patients with relapsed or refractory CLL produced a sustained, durable response.

## Happy New Year

CLL Global would like to take this opportunity to wish each of you a healthy and peaceful holiday season. Though the year has been difficult, we have proven resilient against its challenges. As a community of researchers, clinicians, patients and loved ones, we are stronger and more focused than ever as we work towards a future without CLL. Thank you for being our partner on this journey and for providing us the means to ensure CLL research continues and thrives.



**We wish you the best in the coming year.**



# HOME FOR THE HOLIDAYS



The holiday season is upon us and in pre-pandemic times many of us would be planning parties, vacations, and large gatherings of friends and family around the dinner table. With cases of COVID-19 increasing around the globe, celebrations this year will look a little different. In order to stay safe this holiday season it is important to don a mask everywhere you go, avoid holiday gatherings with non-household members, and socially distance whenever outside the home.

A recent brief issued by the Centers for Disease Control and Prevention found masks do more than just protect the wearer from exhaling particles into the environment, they also protect the person wearing the mask from inhaling particles released by others. Along with hand washing, these actions are important for slowing the spread of the virus and keeping vulnerable populations, including cancer patients, safe this holiday season. In place of crowded in-person festivities, be creative this holiday season and connect with friends and family through virtual gatherings and phone calls.

## THANK YOU HEALTHCARE HEROES

As we come to the close of an unprecedented year, CLL Global would like to say thank you to healthcare workers everywhere for your hard work and dedication. The sacrifices you have made to ensure all patients needing care receive it have not gone unnoticed. We appreciate all that you do on our behalf and we wish you a restful and happy holiday season.



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With COVID-19 cases increasing, online shopping is the way to go this year for your holiday gift shopping. Shop at AmazonSmile and you can give twice the joy. 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. Since 2015, CLL Global has received over \$2,800 through this program.



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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](http://cllglobal.org/donate). Donations may also be mailed to CLL Global Research Foundation, P.O. Box 301402, Unit 428, Houston, Texas 77230.*