



• CHRONIC LYMPHOCYTIC LEUKEMIA •

CLL RESEARCH

2020 Mid-Year Update

CLL Global has provided over \$29.5 million in research funding (2005-2020)

Greetings!

CLL Global is excited to bring you some good news during these incredibly challenging times, and to offer practical advice and hope for the future. The onset of the COVID-19 pandemic early this year disrupted life as we know it on a global scale. Now that we are living with endemic COVID-19, we are required to establish a new normal. As CLL patients, whose immune systems are already compromised, this time has been especially difficult. Fortunately, we now have established safety measures with which to protect ourselves, our clinical teams have learned from experience and are now well informed on how to treat COVID+ CLL patients, and there is evidence that CLL patients taking BTK inhibitors (i.e. ibrutinib) are actually less likely to have severe COVID-19 disease should they get infected.



In spite of disruptions to clinical research resulting from a reallocation of resources during the height of the pandemic, CLL Global has remained steadfast in our resolve to support cutting-edge research aimed at improving the lives of CLL patients and those who love them. Toward this end, we are excited to introduce you to two of our latest grantees, Dr. Philip Thompson and Dr. Nitin Jain, and the promising research they are undertaking. We'll also touch on measures you can take to ensure you stay safe and as healthy as possible until an effective COVID-19 vaccine is available, and offer resources to find answers to questions you may have. But first, a brief word from our founder and friend, Dr. Michael Keating.

We Are Not Done Yet!

G'day. I am writing to you from my home office as I have not been able to go into the hospital these last few months due to safety measures put in place to protect our patients. While this has been difficult for me personally, it has given me an opportunity to think – really think- something my busy schedule has not always allowed. Thinking has renewed my passion and focus on areas of CLL research on which we are lacking information critical to finding a cure and saving countless lives. To some, the fact that we now have non-chemotherapy treatment options that can extend the lives of many CLL patients, potentially for decades, means monetary and research efforts should be focused elsewhere. Well my friends, WE ARE NOT DONE YET! There are many critical questions that need to be answered. We need to understand the genetics behind familial CLL and the onset of second cancers so often seen in patients if we are to successfully prevent these cancers from occurring in the first place, or ensure we catch them at their earliest and most treatable stage. We need to discover what drives Richter's transformation and find therapies for these patients whose outcome is currently very poor. We need better information on how effective vaccines are in CLL patients, especially important as the world is laser-focused on finding a vaccine for COVID-19. Moving forward, state and federal research dollars will be reallocated to address the ongoing COVID-19 pandemic. My promise to you is that CLL Global will steadfastly work towards finding a cure for CLL, funding cutting-edge, out of the box science from some of the greatest research minds in the world. Thank you for making all of this possible. Without your support we would not be where we are today, and we would not have the promise of a world without CLL in our future.

- Dr. Michael Keating

YOUR CONTRIBUTIONS MAKING A DIFFERENCE

It is our pleasure to introduce you to CLL Global's most recent grantees and the exciting research they are doing. Dr. Philip Thompson and Dr. Nitin Jain are exceptional clinician-scientists dedicated to supporting patients and conducting outstanding CLL clinical research.



Dr. Philip Thompson

Dr. Philip Thompson, assistant professor in the Leukemia Department at MD Anderson Cancer Center, was recently awarded funding for his research project, "Evaluating the FCR Cure Fraction - Is the Disease Cured, Dormant or Extinct." Dr. Thompson's interest lies in using minimal residual disease (MRD) as a threshold to determine whether patients need additional treatment, or if they are in fact cured. From his abstract;

"We don't fully understand the significance of very small amounts of MRD (<0.01%). We analyzed one of our FCR studies and found that among patients with undetectable MRD at a sensitivity of 1 cell among 10,000 normal cells (MRD4 - our routine MRD test in the lab), 75% had detectable MRD when we used a test with a sensitivity of 1 CLL cell in 1,000,000 normal cells (MRD6). Patients who were MRD6+ had increased relapse risk. However, some patients with MRD between 0.0001 and 0.01 didn't relapse. Many clinical trials are examining using increasingly sensitive MRD analysis to decide on whether to give additional treatment, so understanding the natural history of low-level MRD+ is very important.

We propose to fully update the clinical follow-up for almost 300 patients who have received FCR (or similar) and, among those who had undetectable MRD4, look for MRD6, yearly, for 5 years. This will enable us to precisely determine what "cure" really means. Do all patients in long-term remissions have undetectable MRD6, or do some have very low levels that remain dormant or only increase very slowly with time? The latter groups are very important to identify as they are at risk of being over-treated (eg. a well-meaning physician gives additional therapy to eradicate the MRD which may not have ever caused the patient any problems)."

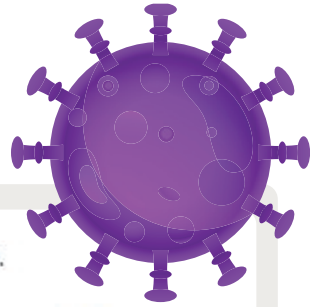
Dr. Nitin Jain, assistant professor in the Leukemia Department at MD Anderson Cancer Center, was recently awarded funding for his investigator-initiated clinical trial, "A Phase II Study of Venetoclax and Ibrutinib in Patients with Chronic Lymphocytic Leukemia." Dr. Jain's research examines the potential of fixed-duration oral therapy for treatment-naïve, as well as relapsed/refractory CLL patients. From his abstract;



Dr. Nitin Jain

"Up until recently, the standard therapy for patients with CLL was with chemotherapy. Several new non-chemotherapy drugs have been identified in the last few years, and more and more patients are now being treated with targeted therapy than chemotherapy. Ibrutinib is an oral targeted therapy currently FDA approved for patients with CLL. However, it is supposed to be taken orally daily indefinitely. Venetoclax is another oral targeted therapy and when combined with an intravenous antibody, it is given for 1 or 2 years. Our group showed that in the laboratory models, the combination of ibrutinib and venetoclax together was very effective against CLL cells. Based on this, we started a clinical trial combining these 2 drugs together (both are oral drugs) for a total of 2 years. We have seen very encouraging responses rates with majority of the patients achieving deep level of remission in bone marrow."

CLL AND COVID-19: WHAT YOU NEED TO KNOW



> [Leukemia](#). 2020 Jul 9;1-10. doi: 10.1038/s41375-020-0959-x. Online ahead of print.

COVID-19 severity and mortality in patients with chronic lymphocytic leukemia: a joint study by ERIC, the European Research Initiative on CLL, and CLL Campus

The first study characterizing the course of COVID-19 in patients with CLL was recently published in the journal *Leukemia* (*Leukemia*. 2020. Jul 9;1-10). This retrospective, international, multicenter study looked at 190 patients with CLL and confirmed COVID-19 in an effort to identify potential predictors of outcome. Findings from this early study showed that, 1) COVID-19 severity increased with age of the patient, 2) CLL treatments, particularly BTK inhibitors like ibrutinib, appeared to have a protective effect, and 3) age and comorbidities did not influence mortality, indicating a relevant role of CLL and immunodeficiency.



VACCINATION

There is good news on the COVID-19 vaccination front. There are five promising COVID-19 vaccine candidates in early phase clinical trials. The candidates have shown the ability to produce antibodies capable of neutralizing the virus, as well as immune cells capable of killing viral infected cells.

How well these vaccines will work in patients with CLL, who have a weakened immune system, remains to be seen, but there is reason to be optimistic. We should know more about the efficacy of these vaccines in mid to late fall of 2020.

In other vaccine news, flu season is just around the corner and with COVID-19 endemic among us it is more important than ever to get your flu (influenza) and pneumonia (pneumococcus) vaccinations. It is possible for a patient to have both flu and COVID-19, a potentially deadly combination, so being up to date is essential.



Having lived with COVID-19 for more than six months now, it is easy to fall into COVID fatigue, slacking on some of the precautions we have been taking. With COVID-19 endemic globally, it is imperative that we continue to follow safety measures including wearing a mask, washing our hands regularly, avoiding crowded spaces whenever possible and social distancing when it is not. These steps have now been proven to be effective at limiting the spread of the virus. And while you are taking care of your physical health, be sure to also take care of your mental health. This is a stressful time for everyone. Being a cancer patient makes it even more so. Take breaks every day – every hour if needed – and do something kind for yourself. Take a walk, practice deep breathing (my personal favorite), practice yoga or read something inspirational. All of these are reminders of the good things in our lives, and help to keep our perspective positive. Together, we will survive and thrive.



Follow us on Facebook to keep up with the latest information on CLL and COVID-19.

**EMTS &
FIREFIGHTERS &
POLICE &
FIRST RESPONDERS &
DOCTORS &
NURSES &
DELIVERY DRIVERS &
ESSENTIAL WORKERS**
Thank You!



THANK YOU TO OUR SUPERHEROES

We would like to close this newsletter with an expression of gratitude to all the essential workers who are going above and beyond to keep us safe during this pandemic. Some are easy to spot on the front lines every day, police and fire, our clinical teams in the hospitals, grocery workers, and some are not as visible, custodial workers, statisticians, and

laboratory technicians. We want these folks to know how immensely grateful we are for the tireless effort they have put forward during this incredibly difficult time. We thank each and every one of them for their hard work and sacrifice. For our part, we promise to continue following recommended safety standards to make their jobs easier. Together we will get through this and not just survive but thrive!



Did you know that you can support CLL Global while you are stuck at home doing all of your 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. In 2019, we received over \$2,500 through the AmazonSmile program.



Our friends at Patient Power – A Cancer Community (www.patientpower.info) are a great source of information about CLL, including the latest on clinical trials, educational information and events for patients and caregivers. During the COVID-19 pandemic, they are hosting multiple “Ask the Expert” sessions, as well as producing up-to-date material from CLL experts on what we know about the impact of COVID-19 on the CLL community. Visit their website for information and to get your questions answered.



• CHRONIC LYMPHOCYTIC LEUKEMIA •

**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.