



• CHRONIC LYMPHOCYTIC LEUKEMIA •

CLL RESEARCH

2021 Mid-Year Update

CLL Global has provided over \$31 million in research funding (2005-2021)

Greetings!

We are halfway through 2021 and what an amazing year it has been so far. News out of the American Society of Clinical Oncology (ASCO) and European Hematology Association (EHA) meetings with regard to CLL has been very positive. Several new drugs and drug combinations currently in clinical trial are showing improved outcomes, including for patients with high risk features. Fixed-duration targeted therapies are likely to see FDA approval in the near future. And while still a real threat, the COVID-19 pandemic is slowly getting under control in many parts of the world and physicians are now better able to manage infections. CLL Global is a driver of these innovations which are leading to a new standard of care for CLL. Our Mid-Year Update highlights some of the ways we are putting your donation dollars to work in our relentless quest to find curative treatment options for all CLL patients.



Congratulations, Dr. Nitin Jain!

Hot off the presses, results published in *JAMA Oncology* showed the combination of ibrutinib and venetoclax to be highly effective in patients newly diagnosed with CLL, including those with high risk features. Patients were treated with ibrutinib and venetoclax for 24 months at which time therapy was stopped. After three years of follow-up the progression-free survival rate was 93%, and 75% of patients achieved undetectable disease in the bone marrow (uMRD) during the study.

For perspective, our best cure fraction as determined by uMRD was 35% just a few years ago. "These long-term results show that two years of oral targeted therapy can achieve lasting disease remission for patients with CLL," said lead author, Dr. Nitin Jain. CLL Global is a proud sponsor of this ongoing research.

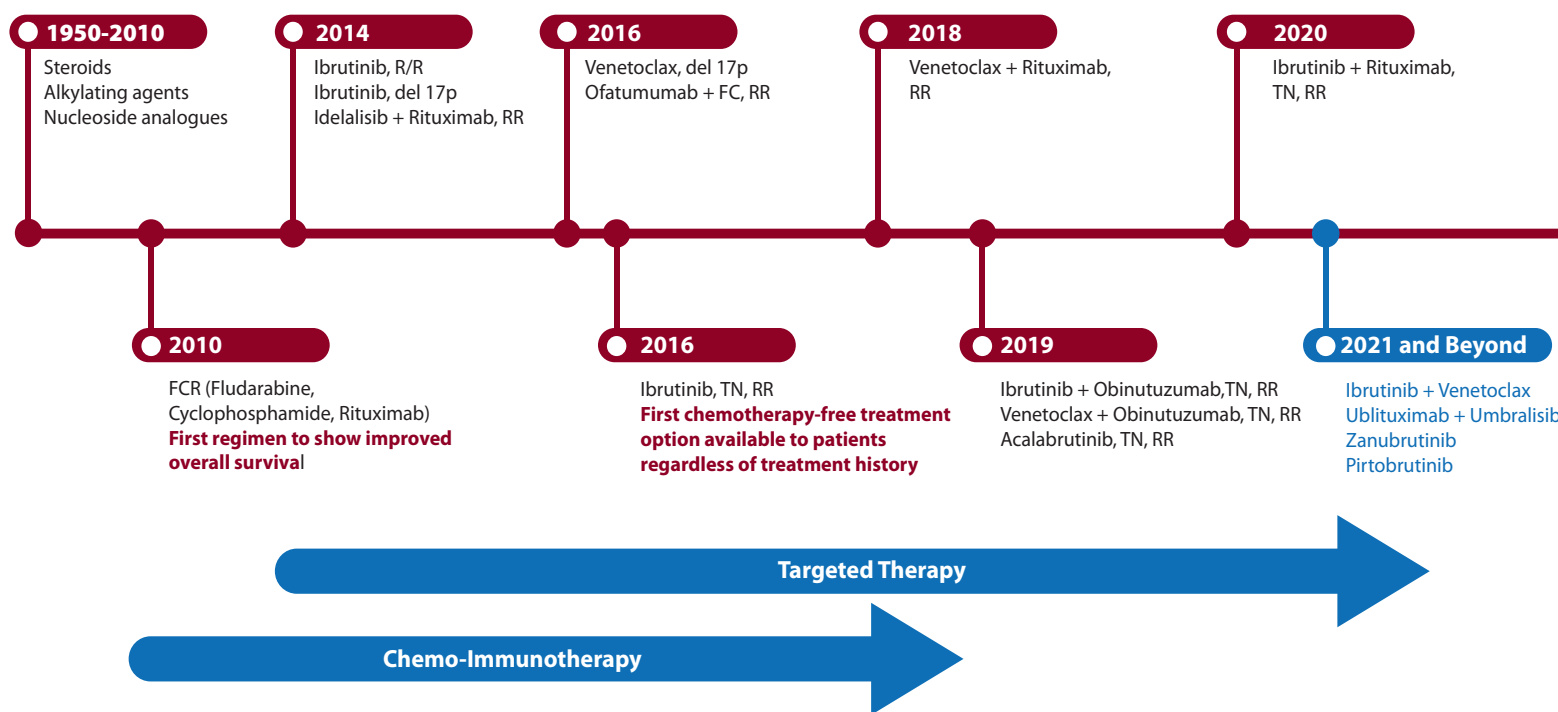
JAMA Oncology | Original Investigation

Ibrutinib Plus Venetoclax for First-line Treatment of Chronic Lymphocytic Leukemia A Nonrandomized Phase 2 Trial

Nitin Jain, MD; Michael Keating, MD; Philip Thompson, MD; Alessandra Ferrajoli, MD; Jan A. Burger, MD, PhD; Gautam Borthakur, MD; Koichi Takahashi, MD, PhD; Zeev Estrov, MD; Koji Sasaki, MD; Nathan Fowler, MD; Tapan Kadia, MD; Marina Konopleva, MD, PhD; Yesid Alvarado, MD; Musa Yilmaz, MD; Courtney DiNardo, MD; Prithviraj Bose, MD; Maro Ohanian, DO; Naveen Pemmaraju, MD; Elias Jabbour, MD; Rashmi Kanagal-Shamanna, MD; Keyur Patel, MD, PhD; Wei Wang, MD, PhD; Jeffrey Jorgensen, MD, PhD; Sa A. Wang, MD; Naveen Garg, MD; Xuemei Wang, MS; Chongjuan Wei, PhD; Nichole Cruz, RN; Ana Ayala, RN; William Plunkett, PhD; Hagop Kantarjian, MD; Varsha Gandhi, PhD; William G. Wierda, MD, PhD

EVOLUTION of FDA-Approved CLL Therapy

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The last seven years have seen unprecedented advances in FDA-approved treatment options for CLL patients with the gradual movement away from chemo-immunotherapy towards newer, targeted therapies. CLL Global and its grantees have been at the forefront of this evolution, and we continue to pave the way for the future by funding cutting-edge pre-clinical and clinical research into new drugs and drug combinations. (R/R = relapsed and/or refractory, del 17p = deletion of chromosome 17p, TN = treatment naïve, 2021 and Beyond = some of the agents currently in clinical trial showing promise).



How Effective Is the SARS-CoV-2 Vaccine In CLL Patients?

Patients with CLL have a suppressed immune system and are more susceptible to infections than the general population. Because of this, the COVID-19 pandemic has been especially difficult for CLL patients to navigate. Thankfully, we now have multiple safe vaccine candidates available, and it is recommended that CLL patients get vaccinated.

What is unknown at this time is how effective the SARS-CoV-2 vaccine is in patients with a suppressed immune system. Data recently published in the journal *Blood** showed the antibody response of CLL patients to the Pfizer vaccine was markedly impaired and dependent on disease stage and treatment.

To more fully investigate this question, CLL Global is actively partnering with Dr. Chaitra Ujjani (pictured above) from the University of Washington and her colleagues across the United States. Her study will analyze 500 CLL patients for their immune response (antibody-based and cellular immunity) to the vaccine over time to determine the level and durability of response. Results from this study will provide critical information to patients and physicians on how to safely navigate endemic COVID-19.

**Blood* (2021) 137(23):3311



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Making a Difference One Dollar at a Time



Contributed over
\$31M to CLL
research since 2005



Sponsored research
published in 212
high impact journals
and cited over
20,000 times



Helped advance 6
of 7 FDA-approved
targeted therapy
options for CLL



Collaborate with
scientists and
physicians on five
continents

Highlighting Our Research Partners: Dr. Deepa Sampath



It is our pleasure to introduce you to CLL Global's most recent grant recipient, Dr. Deep Sampath. Dr. Sampath's research interests lie in the development of novel therapies for patients with high-risk CLL, in particular those with deletion of chromosome 17p and/or TP53 mutation(s).

How did you become interested in CLL research?

When I started a post-doctoral fellowship at MD Anderson Cancer Center with Dr. Bill Plunkett, I began to work with Dr. Michael Keating and the CLL team. It gave me insight into all the exciting advances being made in CLL and I became very interested in CLL research.

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

I am focused on understanding the biology of CLL that has TP53 mutations. TP53 is the gene that encodes the tumor suppressor protein, p53. In the relapsed /refractory setting, having a del17p (loss of 1 TP53 gene) is often accompanied by mutations on the 2nd TP53 gene. These mutations occur all across the TP53 gene. However, not all TP53 mutations have the same impact on prognosis. Some are neutral in effect but others are very deleterious. My goal is to identify therapeutic strategies that are effective in this poor prognosis subgroup.

What question is your research trying to answer?

TP53 is primarily a transcription factor. Mutant TP53 not only blocks the tumor suppressor function of wild-type TP53 but depending on the exact location of the mutation, it can promote disease progression showing a "gain of function" (GOF). My goal is to systematically evaluate the role of each TP53 mutation in CLL samples to determine whether they have GOF activity and determine their consequence on disease progression during ibrutinib or venetoclax therapy.

How will your research translate to the clinic?

Our present work has uncovered a key protein, PKC- β , as a downstream target of mutant p53. When mutant p53 transcriptionally activates PKC- β , BTK inhibitors like ibrutinib can no longer suppress the CLL cell's survival signals and disease progression occurs. Early clinical trials using a compound that blocks PKC- β activity have been promising in CLL, including in patients with del17p.

How will funding from CLL Global benefit your research program?

My grant from CLL Global will allow me to generate preliminary data on the biology of mutant p53 CLL and also to devise rational combinations with PKC- β inhibition. Once in hand, this information will be used to leverage additional funding at the state and national level.

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

When not working, I love spending time gardening or travelling with my husband and two sons.

CLL Global Town Hall

Join us on Thursday, July 29, 2021, from 4:00-5:00 PM Central Time for our first ever CLL Global Town Hall! Speakers for this virtual event will include CLL Global founder, Dr. Michael Keating, our president, Dr. Bill Wierda, and current grant recipient, Dr. Philip Thompson, all from MD Anderson Cancer Center. The event will be moderated by CLL patient and advocate, Jeff Folloder. Hear updates on the latest CLL research presented at this year's ASCO and EHA meetings, learn about some of the ongoing research sponsored by CLL Global, and get your questions answered by the experts. Visit our website at cllglobal.org to register. Registration is free.

The Best Is Yet To Come!

The past ten years have witnessed amazing progress in the control and treatment of CLL and CLL Global has been there every step of the way. From the gradual movement away from chemo-immunotherapy to newer, less toxic, targeted therapies, and now to clinical trials of limited-duration treatment combinations that can induce lasting remissions, CLL Global has championed cutting-edge research that is advancing the CLL narrative. None of this would be possible without the generosity of our extraordinary donors. As the largest nonprofit funder of CLL research, we are honored to partner with you in our unwavering quest for a cure. The best is yet to come!



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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.



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