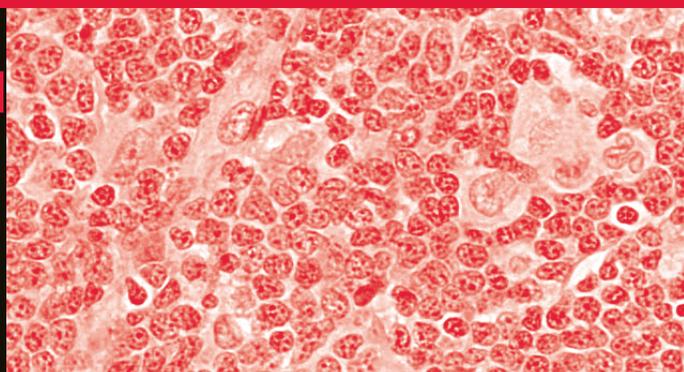


# RESEARCH Report



## Foundation's Oral Therapies Initiative Marks Five Years of Advocacy and Research



(L to R): Christopher Flowers, MD, of Winship Cancer Institute, Emory University, Thomas M. Habermann, MD, of Mayo Clinic, Rochester and LRF Scientific Advisory Board Chair 2017-2019, and Michael Williams, MD, of University of Virginia Health System and Co-Chair, Oral Therapies Steering Committee, attend the Adherence in Oral Therapies Workshop in New York, October 2017. Dr. Flowers is one of the authors of a recent publication from the Foundation's Oral Therapies Initiative, which is marking five years of advocacy in 2019.

Oral Therapies Steering Committee, led by Foundation Scientific Advisory Board members Jonathan Friedberg, MD, MMSc, of Wilmot Cancer Institute, University of Rochester, and Michael Williams, MD, ScM of the University of Virginia Cancer Center, to advocate for greater exploration and research into oral therapies in lymphoma, through both scientific meetings, editorials, and academic publications.

"Oral therapy for lymphoma and CLL has become an important option for many patients," said Dr. Williams, "The appeal of prolonged remission, the perception that it is more convenient and may decrease office visits, and having a greater sense of control over one's own care are all appealing. However, with this shift, all of us involved in lymphoma patient care must pay attention to the efficacy, value, and cost, as well as the convenience of and adherence to oral therapies."

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***"With this shift [to oral therapies], we must pay attention to the efficacy, value, and cost as well as the convenience of and adherence to oral therapies."***

Over the past five years, an increasing number of lymphoma and chronic lymphocytic leukemia (CLL) patients receive their chemotherapy not from intravenous (IV) treatments administered in a hospital or clinic, but via a pill, taken at home on a regular basis, similar to prescriptions for many other health conditions. These oral therapies have become a more standard part of patient care, and for a growing number of patients, oral therapies are their only option. However, issues unique to their use have become concerns for clinicians and researchers in the lymphoma community.

The Lymphoma Research Foundation's Oral Therapies Initiative, founded in 2015 to explore these concerns, recently marked five years of advocacy on these issues with a June 2019 publication in *Leukemia & Lymphoma*, exploring current research into the issue of adherence in oral therapies and making recommendations for future research questions that should be explored to truly understand the effect of various real-world concerns and influences on a lymphoma patient's successful adherence to a treatment plan involving oral chemotherapy. This publication is just the latest effort by the



**FEATURED IN THIS ISSUE: Highlights from 2019 Scientific Conferences**

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Lymphoma Research Foundation grantees and Scientific Advisory Board members (including Ari Melnick, MD of Weill Cornell Medicine, at left) present research at prestigious summer oncology conferences, including the International Conference on Malignant Lymphomas (ICML) in Lugano, Switzerland.

# Letter from the CEO



Dear LRF Friends and Supporters,

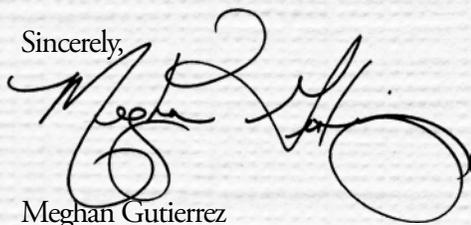
The Lymphoma Research Foundation's research portfolio encompasses not just the grants we fund, but a number of scientific workshops and initiatives designed to bring attention to and encourage collaboration on important issues in lymphoma research and patient care, particularly those that are understudied or related to the quickly changing treatment landscape in lymphoma and chronic lymphocytic leukemia. In this issue of *Research Report*, we highlight several such programs, beginning with our cover article, an overview of the first five years of our Oral Therapies in Lymphoma Initiative. This initiative, which recently published a paper

in the academic journal *Leukemia & Lymphoma*, has raised awareness among the research community and beyond about the unique issues which affect patients who take oral agents for the treatment of their lymphoma.

This spring, the Foundation also hosted two first-of-their-kind scientific workshops on Marginal Zone Lymphoma and Adolescent/Young Adult Lymphomas, two areas of understudied research. A summary of both workshops begins on page 4. In addition, Foundation grantees, Scientific Advisory Board members, and other researchers with Foundation ties presented a number of studies at the American Society for Clinical Oncology (ASCO) Annual Meeting and International Conference on Malignant Lymphoma (ICML), both held in June 2019. Highlights from these presentations begin on page 6.

This edition of *Research Report* showcases the broader impact of the Foundation's research portfolio beyond our annual grant funding. Thank you for all you do in helping the Foundation advance innovative research and improve care for all who are impacted by a lymphoma diagnosis.

Sincerely,



Meghan Gutierrez  
Chief Executive Officer

## Team LRF Spotlight: Team Kweit

**L**ewis Kweit, of New York, NY founded Team Kweit to participate in the New York Lymphoma Walk in memory of his wife, Karen. For the 2019 New York Walk, Team Kweit raised over \$18,000, bringing their two year total to nearly \$50,000, and raising the most funds of any NYWalk team in both 2018 and 2019.

In recognition of Team Kweit's efforts, Lewis and Team Kweit received the prestigious Founder's Award at the 2019 New York Walk from Marnie Gordon, who created the Lymphoma Research Foundation's New York Walk as a volunteer more than twenty years ago.

The 2019 Lymphoma Walk season will conclude with the Chicago Walk on August 4 and the Arizona Walk in Phoenix on October 20. For more information, visit [lymphoma.org/teamlrf](http://lymphoma.org/teamlrf).



Lewis Kweit (R), receives the Founder's Award from Marnie Gordon at the 2019 New York Lymphoma Walk.

## Oral Therapies

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### History of the Oral Therapies Initiative

In 2013, the U.S. Federal Drug Administration (FDA) approved oral chemotherapy agents lenalidomide (Revlimid) and ibrutinib (Imbruvica) for relapsed mantle cell lymphoma, kickstarting a new era in which oral therapies for lymphoma and other cancers have become increasingly standard therapies. In the five years following lenalidomide's approval, six oral chemotherapies have been approved for a range of lymphoma subtypes and seven additional therapies are being investigated in clinical trials for lymphoma.

Although it was hoped that the advent of oral therapies to treat cancer would ease some of the stress, time, and financial burden of the frequent trips to the hospital required by traditional chemotherapy, clinicians and researchers began to have concerns around the real-world use of these therapies by patients. In response to these concerns, the Lymphoma Research Foundation hosted a first-of-its-kind science and policy workshop, *Oral Therapies in Lymphoma*, in Washington, D.C., in September 2015. The workshop, which included clinicians, researchers, pharmaceutical industry representatives, patient advocates, and members of Congress, sought to identify the specific challenges facing the scientific and patient communities related to the development, optimization, treatment adherence, and access to lymphoma oral therapies.

In order to ensure the scientific rigor of the workshop, LRF assembled an Oral Therapies Steering Committee from members of its Scientific Advisory Board. In the five years since that initial workshop, the Committee has continued its efforts to explore the changing nature of lymphoma and chronic lymphocytic leukemia treatment due to



*Jonathan Friedberg, MD of Wilmot Cancer Institute, University of Rochester, and Co-Chair of the Oral Therapies Steering Committee, delivers opening remarks at the Adherence and Oral Therapies in Lymphoma and CLL Workshop in October 2017.*

oral therapies, and advocate for further research into how their use impacts patient care.

The Steering Committee's efforts led to a second workshop, *Adherence and Oral Therapies in Lymphoma and CLL*, hosted in New York City in October 2017, which focused on the complexities of patient nonadherence to oral anti-cancer therapy, including concerns around cost and duration of therapy, misconceptions about the need to continuously take therapy when a patient is asymptomatic, and the impact of comorbidities (other health issues) on the effectiveness of oral therapies due to drug-drug interactions. The workshop also explored how clinicians in diseases that also rely on oral therapies (such as HIV and leukemia) have addressed these issues, and how their models might be adapted for lymphoma.

### Publications and Future Goals

In June 2019, Dr. Friedberg and other members of the Oral Therapies Initiative, including SAB member Christopher R. Flowers, MD, of Winship Cancer Institute, Emory University, and Mary Lou Somma, representing the Foundation's Scientific and Research Programs, published a paper "Maximizing the effectiveness of oral

therapies in lymphoid cancers: research gaps and unmet needs," in the academic journal *Leukemia & Lymphoma*.

The paper offers an overview of the existing research on adherence to oral medications. This research suggests several key influences on oral therapy adherence, including the negative impacts of complex treatment regimens (for example, plans which require several different therapies or a change in dose levels), the rising cost of treatment and insurance co-payments, patients being unable to obtain their lymphoma medication from their regular pharmacy, as well as the positive impact of educational programs for patients and other interventions, such as automatic prompts to take medicine and monitored dosing boxes.

The authors note that overall data available on oral adherence specific to lymphoma patients was limited, and identified research questions that could be pursued to better understand this issue, including addressing the influence of age, gender, health literacy, pre-existing patient perceptions of oral

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## Foundation's Spring 2019 Scientific Workshops Explore Issues in Marginal Zone and Adolescent/Young Adult Lymphomas

**T**he Lymphoma Research Foundation's scientific programs have long sought to promote discussion around pressing issues in research and patient care. In Spring 2019, two new scientific workshops addressed issues in marginal zone lymphoma (MZL) and adolescent/young adult (AYA) lymphomas patient populations.

The Marginal Zone Lymphoma Scientific Workshop, one of the first scientific workshops in the United States to focus exclusively on this rare group of B-cell non-Hodgkin lymphomas, took place April 17 and 18 in New York City. Held in partnership with the International Extranodal Lymphoma Study Group (IELSG), a leader of MZL research in Europe, the workshop brought together an international group of researchers, clinicians, and industry representatives who specialize in MZL, which is in actuality a group of several lymphoma subtypes including mucosa-associated lymphoid tissue (MALT) lymphomas, and forms which occur both in the lymph nodes (nodal) and without (extranodal). These subtypes include lymphomas which occur in the skin (cutaneous), eyes (ocular), salivary glands, and gastric system, making it difficult for a one-size-fits-all treatment approach. Additionally, the small number of MZL patients diagnosed each year complicates researchers' ability to enroll enough patients on standard clinical trials to get statistically significant results.

The workshop, led by Steering Committee Co-Chairs and LRF Scientific Advisory Board members Morton Coleman, MD of Weill Cornell Medicine, and Thomas M. Habermann, MD, of Mayo Clinic, Rochester, presented an opportunity for the group of U.S. and European investigators to share data and hypotheses, as well as to discuss new potential collaborations with the potential to advance the field with large-scale innovative study. The final afternoon of the two-day workshop featured an in-depth discussion of unmet needs in MZL, focusing on four key thematic areas: pathophysiology, etiology and natural history; therapeutic approaches; clinical trial and study design; and diagnosis, assessment, and response. Publications covering the proceedings and ideas from the workshop are currently in process.

"The Lymphoma Research Foundation's Marginal Zone Lymphoma Scientific Workshop gave researchers from six countries the opportunity to do something we rarely get to do – focus exclusively on marginal zone lymphoma and ways we can drive the field forward for this unique group of diseases," said Dr. Habermann, who was also LRF's Scientific Advisory Board Chair at the time of the meeting. "The interactions during the meeting were phenomenal at all levels. It is my hope that the conversations we began at this meeting will lead to collaborations that will in turn lead to a deeper understanding of this complex group of disorders along with more and better treatment options for MZL patients."

The Adolescent/Young Adult Lymphoma Scientific Workshop, held May 14 and 15 in Chicago, marked the expansion of LRF's AYA Lymphoma Initiative, founded in 2015 with support from The Paul Foundation to address research issues unique to adolescent and young adult lymphoma patients, defined by the National Institutes of Health as patients aged 15 to 39. Building on the success of a one-day symposium hosted by the Foundation in September 2015, which subsequently resulted in a publication in *Blood Advances*, the 2019 AYA Scientific Workshop brought pediatric and adult oncologists and lymphoma researchers, regulatory officials, and industry representatives together for a two-day workshop examining the biological, clinical, epidemiological, and health services issues that cause unique complications in both caring for and conducting research on this patient population.

Under the direction of AYA Lymphoma Steering Committee Co-Chairs Kara Kelly, MD of Oishei Children's Hospital and Roswell Park Cancer Institute, and Dr. Habermann, the workshop assembled six panels to discuss the differences between pediatric and adult oncology treatment strategies, biological factors unique to AYA lymphomas, existing clinical trials focused on AYA patients and strategies for developing new trials, how databases and real-world data can be utilized to gain greater insight into AYA patient outcomes, and survivorship issues for a patient group which may live post-lymphoma for several



The Marginal Zone Lymphoma Scientific Workshop Steering Committee hosts the concluding panel of the Workshop. (L to R): Drs. Du, Zucca, Coleman, Habermann, Younes, Thieblemont, Shipp, and Hsi.

## Lymphoma Research Foundation Spring Scientific Workshop Steering Committees

### Adolescent/Young Adult Lymphoma Scientific Workshop Committee

**Kara Kelly, MD** (Co-Chair), Oishei Children's Hospital, Roswell Park Cancer Institute

**Thomas M. Habermann, MD** (Co-Chair), Mayo Clinic, Rochester

**Catherine Bollard, MD, MBChB**, George Washington University, Children's National Medical Center

**Kieron M. Dunleavy, MD**, George Washington University, GW Cancer Center

**Thomas Gross, MD, PhD**, National Cancer Institute, National Institutes of Health

**Tara Henderson, MD, MPH**, The University of Chicago

**Anne S. LaCasce, MD**, Dana-Farber Cancer Institute

**Christian Steidl, MD**, British Columbia Cancer

### Marginal Zone Lymphoma Scientific Workshop Committee

**Morton Coleman, MD** (Co-Chair), Weill Cornell Medicine

**Thomas M. Habermann, MD** (Co-Chair), Mayo Clinic, Rochester

**Ming-Qing Du, MD, PhD**, University of Cambridge

**Eric D. Hsi, MD**, Cleveland Clinic

**Izidore Lossos, MD**, University of Miami

**Margaret Shipp, MD**, Dana-Farber Cancer Institute

**Catherine Thieblemont, MD, PhD**, Hôpital Saint-Louis

(Hôpitaux Universitaires Saint-Louis, Laboisière, Fernand-Widal)

**Anas Younes, MD**, Memorial Sloan Kettering Cancer Center

**Emanuele Zucca, MD**, Oncology Institute of Southern Switzerland, University of Bern and International Extranodal Lymphoma Study Group

## Spring Workshops

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decades.

The workshop concluded with breakout sessions focused on research topics important to the understanding of AYA lymphoma, including biology and epidemiology, future drug development, care delivery and outcomes, and survivorship. Participants in each breakout session identified key themes, unmet needs, and research priorities for their topic before reconvening to discuss their ideas with the full group. The Foundation and the AYA Lymphoma Steering Committee will take these ideas

into account as they develop future programming and projects for the AYA Lymphoma Initiative.

"The Lymphoma Research Foundation's Adolescent/Young Adult Lymphoma Scientific Workshop brought together pediatric and adult oncologists who get too few opportunities to share their knowledge with each other," said Dr. Kelly. "The feedback we've received from the researchers in attendance has been incredibly positive and we are excited to advance the field of AYA lymphoma research."

*Patients and other stakeholders interested in receiving updates when publications from these workshops are available should visit [lymphoma.org/subscribe](http://lymphoma.org/subscribe) to sign up for AYA and MZL specific email updates. If you are already subscribed to LRF you may add AYA and/or MZL updates to your email preferences at that link.*

## News from the Field: Summer 2019 Scientific Conferences

Scientific conferences offer an opportunity for researchers to share the findings of their latest studies and discuss their impact on patient care with other researchers from around the world. In June 2019, two major conferences, one which encompasses all oncology and one focused exclusively on lymphoma, featured a number of presentations from Lymphoma Research Foundation grantees, Scientific Advisory Board (SAB) members and research consultants.

Highlights of those meetings are covered here.

### ASCO

The Annual Meeting of the American Society of Clinical Oncology (ASCO) is one of the largest annual oncology conferences in the world, assembling clinical researchers from across all types of cancer, including lymphoma and chronic lymphocytic leukemia.

The TRANSCEND CLL 004 trial, which investigated new CD19 CAR T-cell therapy lisocabtagene maraleucel (liso-cel) in relapsed and refractory chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL), was presented by Deborah Stephens, DO, of University of Utah, Huntsman Cancer Institute. Dr. Stephens, a 2014 LRF Scholar, noted that in this small scale trial, thirteen of the fifteen evaluable patients achieved a response to treatment (87 percent), with seven patients achieving a complete remission. Ten patients (67 percent) had undetectable minimal residual disease (MRD) within 30 days of their treatment, a measure of remaining cancer cells that can indicate a risk for relapse. These results indicate liso-cel

may be an effective treatment for CLL/SLL patients who relapse following ibrutinib. The trial is still ongoing and enrolling new patients.

► *TRANSCEND CLL 004 data was also presented at ICML by Tanya Siddiqi, MD, of City of Hope, who has assisted the Foundation in the development of patient education materials. LRF grantee Jacob Soumerai, MD, of Massachusetts General Hospital, was also an author on this study.*

Jason Westin, MD, of The University of Texas MD Anderson Cancer Center, a 2015 LRF Scholar, presented results of the Smart Start trial, a first-of-its-kind study investigating a non-chemotherapy treatment regimen to kick off treatment for patients with non-germinal center diffuse large B-cell lymphoma (DLBCL). Sixty enrolled patients received a combination of targeted therapies rituximab (Rituxan), lenalidomide (Revlimid) and ibrutinib (Imbruvica) for two cycles (RLI), prior to a combination of those agents with chemotherapy. Dr. Westin and his colleagues hoped beginning with a chemotherapy-free regimen would improve outcomes and reduce side effects. With 52 evaluable patients, the overall response rate after the RLI cycles was 84.6 percent (44 patients), and the complete response rate was 38.5 percent (20 patients). Dr. Westin further noted that one patient who achieved complete response opted not to continue to the chemotherapy regimen and remains relapse free 18 months after treatment. Additional studies evaluating more cycles of RLI with less chemotherapy are planned.

► *This study was also presented at ICML by Dr. Westin. The ASCO abstract included*

*contributions from former Scientific Advisory Board member Nathan Fowler, MD, also of MD Anderson Cancer Center.*

The ECHELON-2 trial, an international study exploring the treatment regimen A+CHP (brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone) versus CHOP (cyclophosphamide, doxorubicin, vincristine sulfate, and prednisone) in frontline treatment for peripheral T-cell lymphoma (PTCL) patients with disease positive for the biomarker CD30, was presented by Ranjana Advani, MD, of Stanford University, an LRF Scientific Advisory Board member. After seeing significantly improved rates for complete response (68 percent A+CHP to 56 percent CHOP) and objective response (83 percent A+CHP to 72 percent CHOP), Dr. Advani and her collaborators examined whether there was a difference between level of CD30 expression and the response to A+CHP, noting that in subtypes like systemic anaplastic large-cell lymphoma (sALCL) high CD30 expression is universal, but that the expression level can vary among patients with other PTCL subtypes. Although all patients with CD30 expression greater than 10 percent were eligible for the ECHELON-2 study, researchers found most angioimmunoblastic T-cell lymphoma (AITL) patients had CD30 expression levels between 10 and 30 percent, while patients with PTCL not otherwise specified were evenly distributed from levels between 10 and 100 percent. However, researchers found that CD30 expression was not predictive of response, indicating the significant results for A+CHP will be effective for a

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Lymphoma Research Foundation Scientific Advisory Board member Ari Melnick, MD, of Weill Cornell Medicine, presented the Gianni Bonadonna lecture at the 2019 International Conference on Malignant Lymphoma.

wide number of patients with CD30+ PTCL. Researchers noted that given the lack of relationship found here, patients with less than 10 percent CD30+ should also be evaluated.

► This study was also presented at ICML by Tim Illidge, PhD, of the University of Manchester. The ASCO abstract included contributions from SAB members Nancy Bartlett, MD, of Washington University in Saint Louis, Steven Horwitz, MD, of Memorial Sloan Kettering, and Owen O'Connor, MD, PhD, of Columbia University Medical Center.

## ICML

The International Conference on Malignant Lymphoma (ICML), held biannually in Lugano, Switzerland, assembles international experts on the treatment of lymphoma for presentations and in-depth discussion of the latest research as well as pressing issues in the research and treatment of lymphoma and chronic lymphocytic leukemia. At the 2019 ICML, eight research sessions and three case

discussion sessions were chaired by Foundation Scientific Advisory Board members, with an additional two sessions chaired by former SAB members.

Additionally SAB member Ari Melnick, MD of Weill Cornell Medicine, was invited to give the Gianni Bonadonna Memorial Lecture as part of the keynote presentations. In his talk "Precision Epigenetic Therapy for B-Cell Lymphoma," Dr. Melnick discussed common mutations found in DLBCL and follicular lymphoma (FL), and the therapies in development to address their effects on lymphoma

disease progression, both as individual targeted agents and as adjunct to immunotherapy. Dr. Melnick was introduced by the Bonadonna lecturer from 2017, Margaret Shipp, MD, of Dana-Farber Cancer Institute, also a Foundation SAB member.

A number of grantees and SAB members were also invited to give oral presentations of their research, with several highlights below.

Foundation SAB member Ranjana Advani, MD, of Stanford University, presented initial results of a first-in-class therapy for relapsed/refractory non-Hodgkin lymphoma. The therapy, Hu5F9-G4 (5F9) is an antibody targeting CD47, a protein which, when expressed by cancer cells, serves as what the researchers call a "don't eat me" signal, allowing the cells to grow without being attacked by the immune system. Dr. Advani and her colleagues tested 5F9 in combination with rituximab in 22

patients with DLBCL and FL, 90 percent of whom had relapsed or not responded to rituximab alone. The overall response rate was 50 percent, with 32 percent achieving complete response, and the majority of patients experiencing only low-grade side effects. Researchers also reported that 90 percent of patients who responded were still in response, including one patient who had maintained their response without disease progression for over thirteen months. The researchers noted the 5F9-rituximab combination appeared to be both effective and well tolerated, and added that larger scale trials are currently ongoing in both indolent lymphoma and DLBCL.

► This study was also presented at ASCO by Dr. Advani and at the annual meeting of the European Hematology Association (EHA) by Dr. Mark Roschewski, MD, of the National Cancer Institute. The ICML abstract included contributions from SAB members Nancy Bartlett, MD, of Washington University in Saint Louis, Ann LaCasce, MD, of Dana-Farber Cancer Institute, and Sonali M. Smith, MD, of The University of Chicago, as well as past LRF grantee Leslie Popplewell, MD, of City of Hope, and MCL Consortium member Ian Flinn, MD, PhD, of Sarah Cannon Research Institute.

Another new therapy being tested in combination with rituximab was presented by Andrew D. Zelenetz, MD, PhD of Memorial Sloan Kettering Cancer Center, incoming Chair of the Foundation's Scientific Advisory Board. ME-401, an inhibitor of the phosphoinositide 3 kinase (PI3k), was evaluated in an early phase study of patients with relapsed and refractory B-cell malignancies – Dr. Zelenetz's presentation focused on results in patients with FL and CLL/SLL. Of the 43 evaluable patients in FL, 33 (77 percent) achieved an objective response to the

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## Foundation Partners with *Leukemia & Lymphoma Journal* to Highlight Case Studies from LRF Professional Education Programs

The Lymphoma Research Foundation's signature professional education program series, "Lymphoma Rounds," provides a forum for local healthcare professionals to meet on a regular basis and address issues specific to the diagnosis and treatment of their lymphoma patients. Lymphoma Rounds launched in 2008 in Chicago and is currently held in eight markets across the U.S. including Chicago, Los Angeles, New England, New York, Philadelphia, San Francisco, Seattle, and Washington, D.C. – with each market meeting multiple times a year. Participants in the program receive Continuing Medical Education (CME) credits, allowing them to keep their expertise in lymphoma treatment up-to-date.

In April 2019, the Foundation partnered with the academic journal *Leukemia & Lymphoma* to feature select cases from LRF Lymphoma Rounds' programs. Each published case is reviewed by Morton Coleman, MD, and Koen van Besien, MD, PhD, of Weill Cornell Medicine, both Steering Committee members of the New York Lymphoma Rounds program. Dr. Coleman is also a member of LRF's Scientific Advisory Board and Board of Directors, Chair of the Foundation's Medical Affiliates Board, and Lymphoma Rounds founder; Dr. van Besien is a long-time LRF Mantle Cell Consortium member and a current editor-in-chief of *Leukemia & Lymphoma*. The first Lymphoma Rounds case was published in the 18 April 2019 digital issue and focused on the treatment of refractory T-cell prolymphocytic leukemia (T-PLL), a rare T-cell lymphoma. Presented initially at New York



Lymphoma Rounds by Alexandra Gomez-Arteaga, MD, a fellow at Weill Cornell Medicine, and Dr. van Besien, the published case study also featured contributions from Foundation SAB member Steven Horwitz, MD, of Memorial Sloan Kettering Cancer Center. Additional case studies will be published throughout the year.

"As attendance at the Foundation's Lymphoma Rounds programs steadily increases, the Lymphoma Research Foundation continues to identify opportunities to expand the reach of these programs beyond their host cities," said Piper Harmon, Senior Manager of Professional Education Programs. "The Foundation's partnership with *Leukemia & Lymphoma* not only allows the cases discussed at Lymphoma Rounds, often involving rare lymphomas or unusual clinical presentations, to be made available to a wider audience, but offers an opportunity to improve care for lymphoma patients."

*For more information about Lymphoma Rounds and other resources for healthcare professionals, visit [lymphoma.org/professionaled](http://lymphoma.org/professionaled).*

## News from the Field

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ME-401+rituximab combination, and all 11 CLL/SLL patients (100 percent) responded. Additionally, Dr. Zelenetz and his collaborators noted that patients started on an initial daily continuous schedule of the therapy and then switched to an intermittent schedule in cycle three to reduce toxicity, but that patients whose disease progressed while on the intermittent schedule stopped progressing by going back to a continuous schedule. An international study is currently enrolling patients with relapsed/refractory FL that will test different schedules for switching between continuous and intermittent schedules in order to determine the most effective schedule.

► *This abstract also included contributions from current LRF grantee Jacob Soumerai, MD, of Massachusetts General Hospital, and past grantee John Pagel, MD of Swedish Cancer Institute.*

Paolo Strati, MD, of MD Anderson Cancer Center, a 2019 LRF Scholar, presented a retrospective analysis on the value of pre-treatment positron emission tomography (PET) scans for patients with FL receiving their initial therapy. Dr. Strati noted that PET is currently recommended for FL patients for initial staging, evaluation of potential transformation, and response assessment, but that the potential prognostic value of this pre-treatment scan was understudied. Dr. Strati and his colleagues looked at the records of 346 patients who received frontline rituximab based therapy at MD Anderson between 2001 and 2014, looking at the standardized uptake value (SUV), a measurement done in PET scans that helps indicate the amount of cancerous tissue in a patient's body. The researchers found that patients whose pre-treatment

scan showed an SUV of greater than eighteen had significantly shorter progression free survival and complete response rate when treated with a non R-CHOP regimen, but that those treated with R-CHOP had similar rates to patients with lower SUV. However they also found that patients in the greater than eighteen group had shorter overall survival regardless of the therapy given. Noting that R-CHOP is considered a more aggressive treatment than most standard non-R-CHOP therapies, Dr. Strati and his collaborators noted that these data suggest pre-treatment SUV could be used to identify patients that may need the more aggressive course of therapy, but that further studies to confirm these findings are needed.

► *This abstract also included contributions from former SAB member Nathan Fowler, MD, past LRF grantee Jason Westin, MD, and MCL Consortium members Jorge Romaguera, MD and Michael Wang, MD, all of MD Anderson Cancer Center.*

Elise Chong, PhD, of the University of Pennsylvania, the Foundation's 2019 Bruce D. Cheson, MD Postdoctoral Fellow, presented four-year follow-up results from a trial of CD19 chimeric antigen receptor (CAR) T-cell therapy tisagenlecleucel (Kymriah) in relapsed and refractory DLBCL and FL. Dr. Chong noted that eligible patients enrolled in the study had no curative treatment options and a prognosis of less than two years survival at time of enrollment. With the median follow-up now at 49 months, 46 percent of the 24 DLBCL patients and 71 percent of the fifteen FL patients had a complete response. For patients who responded to treatment in either group, the median response duration (the point at which half of the patients have experience disease progression) has not yet been reached, more than four years later. The patient with the longest

follow-up period remains in remission from double-hit DLBCL at 60 months (five years) after their initial CAR-T therapy. Dr. Chong also noted that these results are the longest follow-up results reported to date for tisagenlecleucel in B-cell lymphomas and that for patients with few other options, CAR T-cell therapy continues to offer long-lasting results.

► *This abstract also included contributions from Stephen Schuster, MD of the University of Pennsylvania, a member of the Pennsylvania Lymphoma Rounds Steering Committee.*

Connie Batlevi, MD, PhD, of Memorial Sloan Kettering Cancer Center, a 2015 LRF Scholar, presented early clinical trial data of a second-generation chimeric antigen receptor (CAR) T cell therapy that targets not just the protein CD19, but a second commonly expressed protein, either C2D28 or 4-1 BB. Patients with relapsed or refractory lymphomas including DLBCL, FL, transformed FL, Waldenstrom macroglobulinemia, and CLL including Richter's transformation were eligible to enroll in the study, which sought to evaluate the safety of these CAR T-cells and assess overall response rate. Twenty-seven patients were evaluable for response, with sixteen (59 percent) achieving a complete response; eight of these patients remain in complete response at a median of 169 days following therapy. Researchers noted no severe cytokine release syndrome and three patients with neurotoxicity, but no cerebral edema, indicating low occurrence of common severe side effects for CAR T-cell therapy. Dr. Batlevi and her colleagues indicated further studies of this second-generation CAR T-cell therapy are warranted to gauge if it is a significant improvement on existing therapies.

► *This trial also included contributions from SAB member Anas Younes, MD, and former grantees*

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## Oral Therapies

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therapies prior to treatment, and patient-physician or other healthcare relationships on therapy adherence; the effect of logistical challenges such as drug-drug interactions from multiple health issues, visiting multiple pharmacies to fill prescriptions, and the increased cost of therapies when compared to traditional therapies; as well as identifying not only whether interventions and educational programs significantly alter adherence rates but which types of interventions are most effective.

“Not only is research into this field essential to enhance the experiences of lymphoma patients,” noted the authors in their conclusion, “but it could also apply to a wide range of cancers and diseases that may use oral treatments in the future.”

The *Leukemia & Lymphoma* article marks the fourth publication proceeding from

the Oral Therapies Initiative, which also include:

- *Oral Therapies in Lymphoma: Opportunities and Challenges in Research and Treatment*, a whitepaper proceeding from the 2015 workshop, published in early 2016.
- *Adherence and Oral Therapies in Lymphoma and CLL*, a whitepaper proceeding from the 2017 workshop, published in early 2018.
- “Adherence to Oral Anticancer Treatment: Priorities in Lymphoma and CLL,” a June 2018 editorial in *The ASCO Post* from Drs. Williams and Friedberg, offering an overview of LRF’s efforts and advocating for the development of research and new care models to help patients maximize the benefits of this treatment.

“The work the Lymphoma Research Foundation has done with the Oral Therapies Initiative thus far to support exploration into the issues affecting these therapies has helped bring greater attention to these issues for clinicians as well as patients and their caregivers,” Dr. Friedberg says. “The Oral Therapies Committee members look forward to our continued efforts to explore ways in which we can better understand this complex delivery challenge.”

*In addition to the above publications, the Foundation has developed an Oral Agents in Lymphoma Fact Sheet to educate patients and caregivers on available oral therapies and factors to be aware of when one is prescribed. To download the fact sheet, visit [lymphoma.org/oraltherapy](http://lymphoma.org/oraltherapy). Healthcare professionals can also receive bulk orders of print materials free of charge via [lymphoma.org/professionaled](http://lymphoma.org/professionaled).*

## News from the Field

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*Maria Lia Palomba, and Renier Brentjens, MD, PhD, all of Memorial Sloan Kettering Cancer Center, as well as Craig Moskowitz, MD, of the University of Miami.*

Results of a trial investigating the Bruton’s tyrosine kinase (BTK) inhibitor acalabrutinib (Calquence) in relapsed and refractory CLL were presented by Kerry Rogers, MD, of The Ohio State University. The trial focused on enrolling patients who had developed intolerance to ibrutinib (also a BTK inhibitor), suffering severe or persistent side effects,

and whose disease progressed after discontinuing ibrutinib treatment. Sixty patients were treated, with an overall response rate of 72 percent. Moreover, at a median follow-up of 23 months, 62 percent of patients were able to remain on acalabrutinib, with the majority discontinuing due to progressive disease (thirteen percent); while ten percent of patients discontinued acalabrutinib due to adverse events researchers cited a recent paper noting that the majority of patients who discontinue ibrutinib do so due to intolerance. Dr. Rogers and her collaborators suggested acalabrutinib

may be a safe and effective option for CLL patients who are intolerant to ibrutinib but whose disease responds well to BTK inhibition.

➤ *This abstract included contributions from SAB member Bruce D. Cheson, MD, FACP, FAAS of Georgetown University and former SAB member Thomas J. Kipps MD, of the University of California San Diego.*

*For more News from the Field, visit [lymphoma.org/newstype/research-news](http://lymphoma.org/newstype/research-news).*

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### About the Research Report

*Research Report* is a publication of the Lymphoma Research Foundation, providing the latest updates on our grantees and their progress, as well as on the work of the Foundation. The Lymphoma Research Foundation is the nation's largest non-profit organization devoted to funding innovative lymphoma research and serving the lymphoma community through a comprehensive series of education programs, outreach initiatives, and patient services.

### LRF Helpline

The Lymphoma Research Foundation (LRF) offers a variety of support services to lymphoma patients, survivors, and caregivers. These programs include the LRF Helpline, which provides information about lymphoma and its treatment options, as well as the Lymphoma Support Network for peer support and encouragement. Individuals touched by lymphoma can also learn about novel and emerging therapies through our Clinical Trials Information Service. As part of this program, LRF staff can conduct individualized lymphoma trial searches for patients to assist them in making important decisions about their care. For more information about the Clinical Trials Information Service or any of LRF's support services, please contact the LRF Helpline at 1-800-500-9976 or helpline@lymphoma.org, or visit lymphoma.org/learn/supportservices.

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**Spring Scientific Workshops**

Overviews of the Marginal Zone Lymphoma and Adolescent/Young Adult Lymphoma Scientific Workshops convened by the Foundation.

Visit page 4 for details.

**WE RIDE TO CURE LYMPHOMA. JOIN US.**



Ride Co-founders Dr. Bruce and Christine Cheson

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to help cure lymphoma**

**Sunday, September 22, 2019**  
**Barnesville School, Barnesville, MD**  
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50/40/25/10 mile ride options.  
All ages 12+ welcome.