LYMPHOMA RESEARCH • FOUNDATION

Research Report

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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.

Inside this Issue

FDA Approvals	1
New Grantees	1
Letter from the CEO	2
LCRMP Meeting	5
Scientific Advisory Board	10
Foundation Update	11
News from the Field	12

Breakthrough Lymphoma Therapies Headline Significant FDA Approvals in 2013

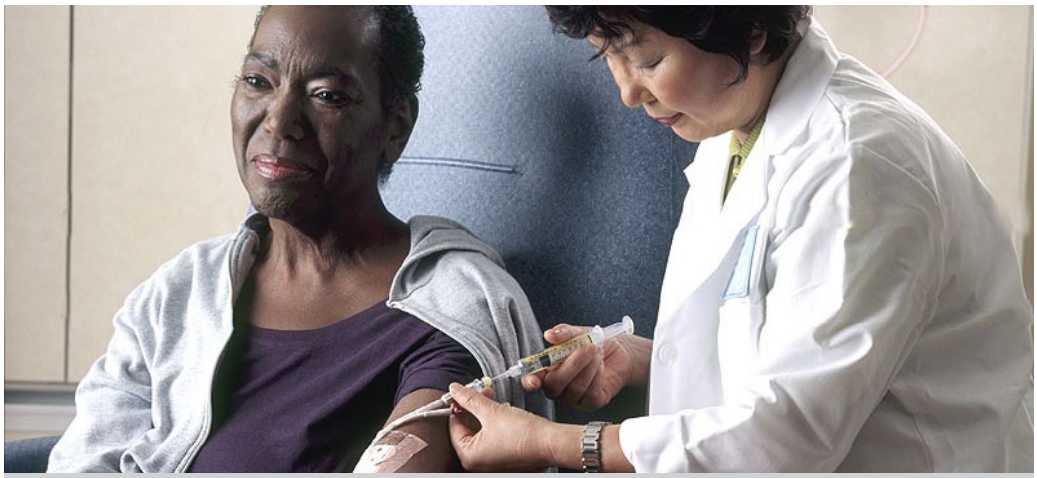


Photo: Rhoda Baer, National Cancer Institute (NCI)

Lymphoma patients now have access to more and better therapies, after 2013 saw several new drugs approved by the United States Food and Drug Administration (FDA). Chief among these approvals were the first two therapies approved under the FDA's new Breakthrough Therapy designation, a program established through the advocacy efforts of the Lymphoma Research

Continued on page 8

Lymphoma Research Foundation Awards over $1 Million to Young Investigators

The Lymphoma Research Foundation (LRF) is pleased to announce the award of thirteen new research grants through its Young Investigator Grants. A cornerstone of LRF's grants portfolio, the Young Investigator Grants have consisted of the Clinical Research Career Development Award (CDA) and Postdoctoral Fellowship grants since 2002. For the 2014 cycle, the Foundation added the LRF Clinical Research Mentoring Program (LCRMP), which provides hands on career development and networking opportunities to early career scientists.

CDAs were awarded to Alexey Danilov, MD, PhD of Dartmouth University and Catherine Diefenbach, MD of New York University, for three years and a total of $225,000. Five post-doctoral fellowships of two years and a total of $105,000 were awarded to Laura Belver, PhD of Columbia University Medical Center, Joseph Dekker, PhD of the University of Texas at Austin, Rui Lu, PhD of the University of North Carolina, Chapel Hill, Feilong Meng, PhD of Children's Hospital Boston, and Oreofe Odejide, MD of Dana-Farber Cancer Institute. The inaugural class of the LCRMP includes six LRF Scholars who will receive grants of $10,000 over two years in addition to hands on mentoring and professional development opportunities (for more on this

Continued on page 2

Dear Friends,

Greetings! What an exciting time this is for the treatment of lymphoma--with several promising new drugs receiving FDA approval, 2014 will offer even more new treatment options. The Lymphoma Research Foundation's (LRF) advocacy efforts were instrumental in helping establish the FDA's Breakthrough Therapy designation – under which both ibrutinib and obinutuzumab received accelerated approval. You can read more about these exciting new developments beginning on page 1.

In January, LRF began accepting applications for our Adolescent/Young Adult (AYA) Cooperative Group Correlative Grant. This new grant seeks studies that will specifically focus on diagnosis, treatment, and outcomes for AYA lymphoma patients (generally designated as ages 15-39), an understudied population whose survival rates, particularly in non-Hodgkin lymphoma, lag behind other age groups. The application period will be closing as we go to press; we will bring you profiles of those grantees later this year.

We are, as always, proud to present our newest group of Young Investigator grantees. This year, our Clinical Research Career Development Award (CDA) and Postdoctoral Fellowship grantees are joined by the first class of the LRF Clinical Research Mentoring Program (LCRMP). These LRF Scholars participated in the inaugural workshop at the beginning of February, launching what we hope will be an invaluable source of support and guidance for lymphoma researchers in the early stage of their careers. Our grantee profiles begin on page 1; for more on the LCRMP, turn to page 5.

On behalf of the Board of Directors and staff at LRF, thank you for your continued support and dedication to our mission as we move forward in our efforts to eradicate lymphoma. Together, we are making a difference!

Yours in purpose and progress,

Elizabeth Thompson
Chief Executive Officer

New Grantees

continued from page 1

program, see page 5). This brings the total awarded through the Young Investigator Grants program to $1,035,000 for 2014 and almost $19 million since 1992.

"One of the greatest investments that LRF and its donors can make is to support the careers and projects of young lymphoma investigators early in their careers," said John Leonard, MD of Weill Cornell Medical College and LRF Scientific Advisory Board (SAB) Chair. "These grants are ultimately leveraged to accelerate the careers and work of these individuals. We expect that they will go on to make many decades' worth of research and clinical care contributions to lymphoma patients that will go far beyond this 'seed' funding."

Clinical Research Career Development Award

Established in 2002, the CDA supports clinical researchers within five years of the completion of their postdoctoral training. Grantees must spend at least 35 percent of their time in independent clinical research; they receive $225,000 over three years for salary support, professional development, and research expenses.

Alexey Danilov, MD, PhD

Dartmouth University Medical Center
Lebanon, NH

Dr. Danilov's grant will help him develop and run a clinical trial investigating a novel agent for CLL.

After receiving his MD and PhD from Yaroslavl Medical Academy in Russia, Dr. Danilov became interested in chronic lymphocytic leukemia (CLL) research as a Research Scholar in Dr. Brigitte Huber's laboratory at Tufts University. "In addition to having a passion for the field of hematologic malignancies, the ability to work with primary samples obtained from patients with CLL has been particularly attractive to me, implying immediate relevance of my research to the clinic," he says. He carried that interest through his residency at Brown University School of Medicine and a Hematology/Oncology fellowship at Tufts before taking his current position as Assistant Professor of Medicine at Dartmouth-Hitchcock Medical Center in New Hampshire. Now his CDA will help him initiate a clinical trial of MLN4924, a drug which targets a specific enzyme common to CLL tumors.

Dr. Danilov's project focuses on the tumor microenvironment for CLL, which contains many genetic proteins that signal cancerous cells to grow and multiply. Many of these signals travel through a pathway called NF-kappaB. MLN4924, the drug Dr. Danilov will be testing, targets the NF-kappaB pathway; the hope is that inhibiting the pathway from signaling the cancerous cells will slow or prevent tumor growth while other drugs used in combination eradicate the malignant tissue. As NF-kappaB has not yet been successfully targeted in the clinic, Dr. Danilov's project could lead to an entirely new class of therapies for CLL.

Noting that the CDA is his first extramural peer-reviewed funded award, Dr. Danilov says he is "particularly excited" about running the early stage clinical trial of this drug. "I truly believe [it] will transform the lives of CLL patients in the near future." He adds that the salary support provided by the grant gives him "protected time" to develop his research. "I will be able to continue submitting proposals and further expand my laboratory, identifying new molecules and drug combinations which will improve the lives of patients with lymphoma."

Dr. Danilov acknowledges that the support of mentors and colleagues has been crucial to his early success. He credits Dr. Jennifer Brown, his mentor on his CDA project, and Dr. Alan Eastman with helping him develop his proposal for LRF. He also thanks his mentors through ASH's Clinical Research Training Initiative– Drs. Kristie Blum, Christopher Flowers, and John Leonard, all LRF SAB members. Calling himself "blessed to be part of a vibrant scientific community at Dartmouth," Dr. Danilov also singles out his lab companions Claire Godbersen and Cody Paiva. "Above all," he adds, "I would like to thank patients who come to participate in Dartmouth clinical trials from the far corners of Vermont and New Hampshire and make progress possible. I have great awe and respect for their spirit and determination to beat cancer on both personal and global levels."

Catherine Diefenbach, MD

New York University
New York, NY

Dr. Diefenbach is developing a clinical trial investigating focal radiation therapy in combination with an immune activating agent for CTCL patients already receiving HDACI.

Many types of lymphoma survive and grow by suppressing the patient's immune system, tricking it into tolerating cancer growth instead of targeting the lymphoma cells for elimination. Dr. Diefenbach is working to develop novel immune based therapies for these patients. Her LRF funded project is a clinical trial investigating the use of focal radiation therapy in combination with an immune activating agent for patients with advanced stage cutaneous T-cell lymphoma (CTCL) that are also receiving histone deacetylase inhibitors (HDACI). "Although HDACI are first line treatment in [CTCL], in many ways they impair immune function" she notes. "My research focuses on whether providing stimulation to the immune system for patients receiving HDACI can improve circulating immune cells in the body and ultimately improve a patient's response to the treatment."

Dr. Diefenbach received her MD and a Masters in Bioethics (MBE) from the University of Pennsylvania before completing her residency at Johns Hopkins Hospital and her Fellowship at Memorial Sloan-Kettering. Currently an Assistant Professor of Medicine at the New York University Langone School of Medicine, she was drawn to lymphoma for both the research possibilities and disease biology – particularly the relationship between the immune system and lymphoma – as well as the patients. "I often feel that being a lymphoma doctor has the best aspects of being a primary care doctor, with the added excitement of a challenging and complex disease, and fascinating research questions," she says. She adds that the variety of new therapies being brought to the clinic makes this a "tremendously exciting time" for clinical researchers in lymphoma. "Learning which of these new therapies will work best with which lymphomas, and how to combine these therapies to achieve maximum clinical benefit with minimal toxicity will be challenging and rewarding work."

Continued on page 4

New Grantees
continued from page 3

Like several of her fellow grantees, Dr. Diefenbach notes that support from the LRF is vital to obtaining both the resources and the protected time to develop as a researcher. She also thanks her "many wonderful mentors and collaborators," including Dr. Ionnis Aifantis and SAB members Drs. John Leonard, Steven Ansell, Brad Kahl, and Ranjana Advani. "I am looking forward to gaining more involvement with the LRF and its programs, broadening collaborations with others in the field, and hopefully in time developing the skills that will allow me to return the incredible support I have received by becoming a mentor myself."

Postdoctoral Fellowships

A part of LRF's grants portfolio since 1992, Fellowships support investigators who have completed two years of their institutional fellowship and no more than two years of their first faculty position. Grantees must spend at least 80 percent of their time in research and receive $105,000 over two years for salary support, professional development, and research expenses for projects that study lymphoma in either the clinic or laboratory.

Laura Belver, PhD

Institute for Cancer Genetics
Columbia University
New York, NY

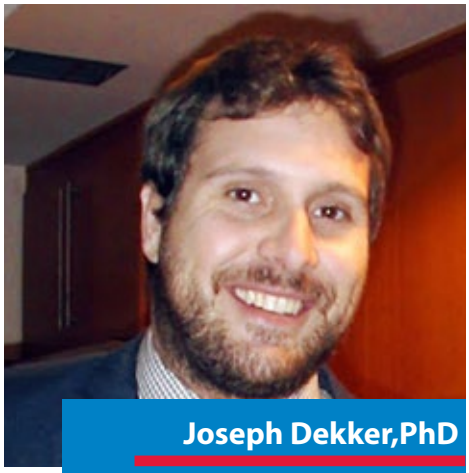
Dr. Belver is investigating the role played by the mutation of the gene NOTCH1 in CLL formation and progression.

The genomics of cancer is a rapidly expanding field of medical research, as scientists work to identify the genes that, when mutated, cause the formation or growth of specific types of cancer. Recently, researchers have identified mutations in the gene NOTCH1 as particularly important to many CLL tumors, including the 30 percent of CLL patients who develop the very aggressive form known as Richter's syndrome. In an effort to better understand how NOTCH1 mutations affect CLL tumor growth, Dr. Belver and her collaborators have developed a genetically modified mouse model of CLL with NOTCH1 mutations. She will spend the two years of her LRF Fellowship using this model to characterize the molecular and cellular functions of NOTCH1 and determine how its mutation impacts CLL cells.

"We believe that our results will provide important novel information on the pathogenesis of CLL, in particular on the most aggressive forms of this disease," Dr. Belver says. "Moreover, the generation of an animal model of NOTCH1-driven CLL will be instrumental to test the efficacy of novel drugs and drug combinations for treatment of CLL patients."

Dr. Belver has been interested in science since she was a young child. "I was always curious about how things work, in particular living beings. That is why I decided to study biology and biochemistry," she says. While completing her PhD in molecular biology at the Autonomous University of Madrid, Spain, she worked under Dr. Almudena Ramiro in basic B-lymphocyte biology. She credits Dr. Ramiro's enthusiasm for the field with furthering her interest in B-lymphocytes and the mechanisms that can cause their cells to transform into malignant lymphomas. "When I got my degree, I decided to continue my scientific career in translational research in oncology, where I could use what I had learned during my PhD about basic research in immunology to find out ways to fight hematological malignancies." Currently a Postdoctoral Research Scientist at the Institute for Cancer Genetics at Columbia University, Dr. Belver sees her CLL research as an extension of her early interest in B lymphocytes.

"I am truly grateful to the LRF that I was given the opportunity to receive this fellowship," Dr. Belver says, adding that the funding provides crucial economic support for her research for the next two years. "I love science and I really enjoy my job. And most of all, I feel truly lucky that my work can help people somehow."



Joseph Dekker, PhD

University of Texas at Austin
Austin, TX

Dr. Dekker is developing a mouse model to explore whether FOXP1 overexpression causes ABC-DLBCL.

Diffuse large B-cell lymphoma (DLBCL) is one of the most common forms of non-Hodgkin lymphoma; a type of DLBCL known as Activated B-Cell (ABC-DLBCL) is one of the most aggressive and difficult to treat forms of this lymphoma. Recent research indicates that when human cells produce too many copies, or overexpress, the gene FOXP1, it often indicates the presence of ABC-DLBCL. FOXP1 is also known to control several other genes which aid the growth of lymphoma cells,

Continued on page 6

LRF Clinical Research Mentoring Program Welcomes First Class

This year's Young Investigator Grants included the first class of LRF Scholars, six early career scientists who were selected to participate in the inaugural LRF Clinical Research Mentoring Program (LCRMP). At the beginning of February 2014, the LRF Scholars, along with a robust faculty of experts in lymphoma clinical research, gathered in Scottsdale, Arizona, for a four-day workshop.

The LCRMP workshop began with each Scholar presenting a proposed clinical research project to the faculty. Each afternoon of the workshop was spent in small groups including experienced clinical researchers and a statistician, allowing the Scholars to receive feedback on the practical design of their projects as well as the underlying science. When not in small groups, the faculty presented didactic lectures on a variety of topics, including basic statistical design for clinical trials, working within the NCI Cooperative Group structure, building a multidisciplinary team for implementing a clinical protocol, and navigating conflict of interest issues. Other presentations featured career development tips such as what to expect in an interview for a faculty position, and how to avoid burnout in the long interval between being a "young" investigator and obtaining a senior position. Faculty presented not only tips for being successful in these areas, but explained their own failures and how to regroup and learn from mistakes and setbacks.

On the final day of the workshop, select faculty presented samples of their own work, which included technologies, genetic pathways, and drugs in development that will likely help define lymphoma research in the coming years. The Scholars concluded the program by presenting the revised versions of their projects for further questions and comments from the faculty.

Early responses from the Scholars and LCRMP faculty have been enthusiastic. "It was a very worthwhile experience and I think it will provide a great advantage to my future career," said LRF Scholar Deborah Stephens, DO of Ohio State.

The inaugural class of LRF Scholars will participate in follow up activities over the next two years; they also received a grant of $10,000 over those two years to cover professional development and small research expenses. LRF is proud to count these promising researchers among their young investigator grantees. ■

(L to R): Deborah Stephens, Ryan Cassaday, Jonathon Cohen, Anita Kumar, Catherine Lai. Not pictured: Joshua Brody.

2014 LRF Scholars

Joshua Brody, MD, Assistant Professor, Icahn School of Medicine at Mount Sinai
Flt3L-primed in situ vaccination for low-grade lymphoma: a pilot study

Ryan Cassaday, MD, Senior Clinical Fellow, University of Washington
Safety and Efficacy of Brentuximab Vedotin Added to ICE for Relapsed/Refractory Hodgkin Lymphoma

Jonathon B. Cohen, MD, Assistant Professor, Winship Cancer Institute, Emory University
A Phase I/II Study of MLN9708 and Ibrutinib in Patients With Relapsed Mantle Cell Lymphoma

Anita Kumar, MD, Medical Oncology Fellow, Memorial Sloan-Kettering Cancer Center
A Pilot Study to Assess the Feasibility of Eliminating Radiotherapy in Bulky Early Stage Hodgkin Lymphoma

Catherine Lai, MD, MPH, Clinical Oncology Fellow, National Cancer Institute, Center for Cancer Research
Short Course EPOCH-RR for Germinal Center B-cell Diffuse Large B-cell Lymphoma

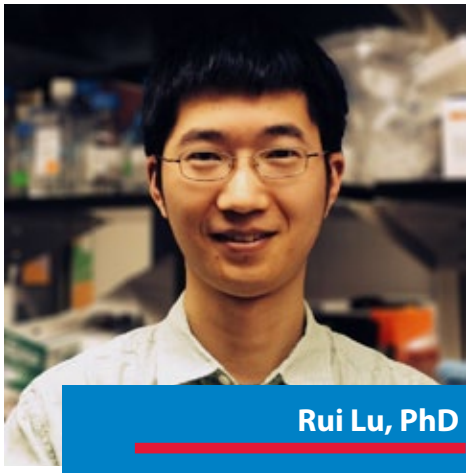
Deborah Stephens, DO, Clinical Fellow, The Ohio State University
A Phase I Trial of Selinexor and Ibrutinib in Relapsed/Refractory CLL and Aggressive NHL

New Grantees
continued from page 4

but it is not fully clear if FOXP1 mutations or overexpression directly cause this type of lymphoma. Dr. Dekker will use his fellowship period to determine genetic pathways important to the development and maintenance of ABC-DLBCL. Ultimately, he will attempt to develop a mouse model of FOXP1 overexpression to determine if the mice develop tumors resembling human ABC-DLBCL. He notes that a mouse model will "greatly accelerate the process" of understanding the underlying biology of ABC-DLBCL. "Such understanding will lead to better diagnosis and illuminate novel targets for new therapies that will better treat these diseases with fewer side effects and more success."

Dr. Dekker received his PhD in immunology and gene therapy from the University of Texas at Austin, where he is now a Postdoctoral Fellow. He was drawn to lymphoma research because of his interest in the immune system and its development. "Lymphoma is a cancer of cells from the immune system that have become dysregulated," he says. "Understanding normal versus dysregulated development and maintenance of these immune cells has become a passion of mine." Dr. Dekker notes that the LRF Fellowship gives him the opportunity to purse a project he has wanted to undertake since receiving his PhD. "It is my first opportunity to contribute something great to the field … LRF has given me the opportunity to prove myself in the field of my choice."

Dr. Dekker receives inspiration for his work from his mother, a breast and ovarian cancer survivor currently undergoing treatment for a recurrence of her ovarian cancer. "Although lymphoma is a different disease, I understand what friends and families are going through upon diagnosis and throughout treatment," he says. His hope is that, over the course of his career, he can further the understanding of lymphoma and its treatment to improve survival rates for even the most aggressive subtypes. "I want to aid in changing the feelings generated during a day of diagnosis from frightening to hopeful and days of treatment from painful to comfortable."



Rui Lu, PhD

University of North Carolina
Chapel Hill, NC

Dr. Lu is developing an inhibitor for the EZH2 and EZH1 genetic pathways in DLBCL.

Genetic mutations of the protein EZH2 are common to certain lymphoma subtypes such as diffuse large B-cell lymphoma (DLBCL). Though researchers have recently developed a few EZH2 inhibitors to treat lymphoma, there are still opportunities for new therapies that more completely inhibit the EZH family enzymes and minimize the side effects of existing inhibitors. Dr. Lu and his collaborators seek to develop an inhibitor that works across both EZH2 and EZH1 in DLBCL. This first-in-class therapy represents a new approach to the inhibition of EZH family enzymes, which may be useful for up to 80% of DLBCL and other B-cell tumors. "We are hoping that our research will help to understand the EZH2 associated epigenetic events in the development of lymphoma," Dr. Lu says.

Dr. Lu received his PhD in developmental biology from the Chinese Academy of Sciences in Shanghai before coming to the University of North Carolina to begin his postdoctoral work in blood cancer and epigenetics. His lab's initial focus was identifying novel factors that bind to chromatin, the complex of DNA and proteins at the nucleus of human cells. This led them to EZH2 and from there to its crucial role in lymphoma. Dr. Lu notes that the Fellowship will allow him to further shift his research focus to epigenetic therapies of lymphoma and other hematological malignancies. "This support from the Foundation will provide a tremendous boost to my research and to my career objective, which is to become a future leader in epigenetic therapies of blood cancers." He credits his mentor, Dr. Greg Wang, with inspiring him to pursue this career path.

"I am really honored to receive an LRF grant," Dr. Lu says, noting that during the funding period he will be able to acquire new knowledge, methodologies, and skills that will allow him to further develop as a researcher, while the connection with LRF specifically will help him and his lab further their connections with the lymphoma research community. "We are excited to see our research could promote better understanding of human cancer such as lymphoma."

Feilong Meng, PhD

Children's Hospital Boston
Boston, MA

Dr. Meng is investigating the protein AID and its role in both antibody production and the generation of lymphoma.

When the human body is infected with a foreign pathogen, the protein

Activation-Induced cytidine Deaminase (AID) signals the immune system to generate better antibodies to neutralize the pathogen. However, if AID reacts too strongly or targets the wrong genes, it can cause the genetic mutations that lead to cancer, particularly B cell lymphomas. Dr. Meng's project is investigating the mechanisms that regulate AID activity. "These studies should enhance our understanding of how AID collateral damage, such as deleterious off-target mutations, DSBs, and chromosomal translocations are minimized," Dr. Meng says. "The result should lead to a greater understanding of molecular pathways that lead to B cell lymphoma and thereby contribute to the development of new therapeutics."

Dr. Meng received his PhD in biochemistry and molecular biology from Shanghai Institutes of Biological Sciences before coming to Boston and becoming a Research Fellow at Harvard Medical School and Children's Hospital Boston. He began working on the AID protein at the beginning of his postdoctoral work, which led him to investigate the questions of how the damage caused by AID to other genes is minimized when the immune system works normally and how it contributes to lymphomagenesis when a malfunction occurs. He is excited at the possibilities offered by LRF funding. "The fellowship definitely will accelerate my research progress," he says noting that the financial support not only covers two years of essential training, but "as an LRF fellow, I get the opportunities to present my work to the lymphoma research community and make connections."

Because Dr. Meng's research is laboratory based, he hadn't interacted directly with lymphoma patients until a close friend was recently diagnosed with follicular lymphoma. "It made me realize how important lymphoma research is and also motivated me to commit to lymphoma research because it can save patients like my friend," he says. "With the support of the LRF fellowship, I hope [my team] can achieve all the proposed goals and get deeper understanding of lymphomas."

Oreofe Odejide, MD

Dana-Farber Cancer Institute
Boston, MA

Dr. Odejide is studying current practices and possible improvements to end-of-life care for lymphoma patients.

Although the mortality rates of lymphoma have improved significantly in recent years, approximately 25 percent of patients still die from this disease. In the course of Dr. Odejide's clinic work, she noticed a lack of data on patients who reach the end-of-life stage and their standards of care. "Only minimal data exists on how to improve end-of-life care for patients with lymphoma," she says, "this attracted me to developing a research plan to investigate factors influencing care near the end of life with the goal of improving the quality of care of lymphoma patients who have not been cured."

Dr. Odejide's project seeks to identify barriers to quality care and possible areas for improvement of end-of-life care for lymphoma patients by surveying clinicians – beginning with a focus group and then using the factors identified there to develop a physician survey that can be more widely distributed. This will be supplemented with an examination of patient data seeking to identify end-of-life factors specific to different subtypes of lymphoma. "I am confident that achieving the aims of this project will lay the groundwork for further research regarding targeted interventions to improve care for lymphoma patients," Dr. Odejide says.

Currently a Hematology/Oncology Fellow at Dana-Farber Cancer Institute, Dr. Odejide received her MD from Howard University College of Medicine before completing her internship and residency at Brigham and Women's Hospital in Boston. She has also received a Certificate in Clinical Effectiveness from Harvard School of Public Health. She credits two of her mentors, Dr. Gregory Abel and LRF Scientific Advisory Board member Dr. Ann LaCasce, with inspiring her commitment to lymphoma patients and helping her acquire the skills necessary to a medical research career. "My progress in lymphoma research is a testament to how much Drs. LaCasce and Abel have invested in me," she says. Having already participated as a speaker in LRF's New England Lymphoma Rounds, Dr. Odejide is looking forward to the new collaborations she hopes to initiate through her research. "I am most excited about the opportunity...to engage with lymphoma clinicians around the country in the discourse of ways to improve quality of care for lymphoma patients."

Dr. Odejide further notes that receiving LRF funding will provide a boost at a crucial time in her career. "The Fellowship is pivotal in launching my research career as it protects my time to focus on my research agenda," she says. "LRF will contribute to my research progress by laying the essential foundation I need to eventually become an independent investigator."

Continued on page 9

To support LRF's research initiatives, visit **community.lymphoma.org/supportresearch**

FDA Approvals
continued from page 1

Foundation (LRF) and other health research organizations to encourage the development of treatments for rare diseases. Whether a brand new, ground-breaking treatment or a known drug redeployed in a new way, promising new options now exist for thousands of lymphoma patients.

Breakthrough Therapies Bring Quick Returns for Lymphoma

The Breakthrough Therapy designation was established by the FDA in 2012 as mandated by the Food and Drug Administration Safety and Innovation Act (FDASIA) signed into law in July of that year. Prior to FDASIA's passage, LRF staff and members of its Advocacy Program met with members of Congress and their staffs to explain the issues surrounding the treatment of rare diseases and encourage the creation of a mechanism to bring new therapies for those diseases to the public more quickly. This issue was particularly important to LRF because patients with several subtypes of lymphoma have few treatment options, and even fewer if those existing treatments fail. Researchers are developing several promising new drugs for those subtypes, but the immense time and financial commitment required to develop through the standard process – estimated at 10-15 years and 1.5 billion dollars – raised the possibility of many of these drugs being abandoned in the development stages. The Breakthrough Therapy designation, which is awarded by the FDA only to drugs for serious or life-threatening conditions that show possible substantial improvement over available therapies, allows a drug's sponsor to receive additional guidance, priority review, and accelerated approval from the FDA. The program offers hope that a faster return on the investment for therapies to treat rare disease will result in more therapies for rare conditions reaching the public faster.

On November 1, 2013, obinutuzumab (Gazyva) became the first Breakthrough Therapy approved by the FDA, for use in combination with chlorambucil to treat previously untreated chronic lymphocytic leukemia (CLL). Clinical studies leading up to the approval found that the addition of obinutuzumab to the standard treatment of chlorambucil increased progression free survival to an average of 23 months, a marked improvement over the average of 11 months offered by chlorambucil alone. Only two weeks later, on November 13, ibrutinib (Imbruvica) became the second approved Breakthrough Therapy, for mantle cell lymphoma (MCL) patients who have received at least one prior therapy. Ibrutinib, which has since been approved for CLL in February 2014, is currently in clinical trials for a number of other B-cell lymphomas, many of which are facilitated by members of LRF's Scientific Advisory Board (SAB). Its approval in MCL comes just seven years into the development process, demonstrating that the Breakthrough Therapy program is already fulfilling its promise of shortening the development timeline.

Old Drugs, New Treatments

Sometimes the most promising new treatment is one that's already known in another form. The FDA approved two treatments for lymphoma in 2013 that were already well known to doctors – one commonly delivered to the patient in a different form, one which was already in use for a different disease.

The oral therapy lenalidomide (Revlimid), already approved to treat multiple myeloma and myelodysplastic syndromes, received approval for patients with relapsed or refractory MCL on June 5, 2013. LRF SAB member Andre Goy, MD, MS of John Theurer Cancer Center, was a key director of the clinical trials which resulted in lenalidomide's approval for this new indication. Because the approval is specifically for MCL patients who have relapsed or failed to respond to at least two prior therapies, one of which includes bortezomib, it offers new hope to a group of patients who had very limited treatment options.

Patients with cutaneous T-cell lymphoma (CTCL), a form of lymphoma that affects the skin, often receive mechlorethamine in the form of an injection underneath the skin. On August 26, 2013, the FDA approved Valchlor, a gel form of mechlorethamine that can be applied topically for stage IA and IB mycosis fungoides-type CTCL. Although some patients have been able to obtain access to mechlorethamine gel as a pharmacy-compounded treatment, these treatments can be inconsistent in quality and effectiveness because they do not require FDA approval and oversight. The FDA approval makes Valchlor the first widely available topical mechlorethamine therapy.

A Big Step Forward, With More to Follow

2013 was a year of great promise for many lymphoma patients, bringing access to several significant new therapies, most of which provide alternatives for patients for whom existing therapies have been ineffective.

LRF Advocates are helping shape policy for lymphoma patients.
Learn more at
lymphoma.org/advocacy

As we move into 2014, treatment options should expand even further. On February 12, 2014, ibrutinib was approved for CLL patients who have received at least one previous therapy. Idelalisib, which has received the Breakthrough Therapy designation for CLL, has also filed for approval in indolent non-Hodgkin lymphoma (iNHL). Through the efforts of both affiliated researchers and the advocacy program, LRF is proud that lymphoma patients will be among the first to benefit from this program. "The creation of the breakthrough therapy designation demonstrated a commitment by lawmakers and the Food and Drug Administration to making treatments available to people with rare diseases, like lymphoma," said Meghan Gutierrez, LRF Chief Program, Policy and Communications Officer. "The new program has already shown, in a relatively short period of time, its ability to expedite the review and approval for new therapies, bringing potentially life-extending treatments to patients." ■

New Grantees
continued from page 7

Summary

The Young Investigator Grants remain a vital part of LRF's commitment to advancing research in lymphoma. These projects offer potentially significant additions to the understanding of lymphoma's development and treatment. In a funding environment where funding for junior research positions is increasingly scarce, the salary support provided by the Career Development Awards and Postdoctoral Fellowships is vital to many of these recipients, while the guidance provided through the Clinical Research Mentoring Program will help its participants launch their careers as independent researchers with a strong support network and crucial professional skills. LRF is proud to support these early career scientists and the promise of the next generation of lymphoma researchers. ■

FDA & Lymphoma: A Recent Timeline

2012

July — FDASIA signed into law; FDA establishes Breakthrough Therapy designation

2013

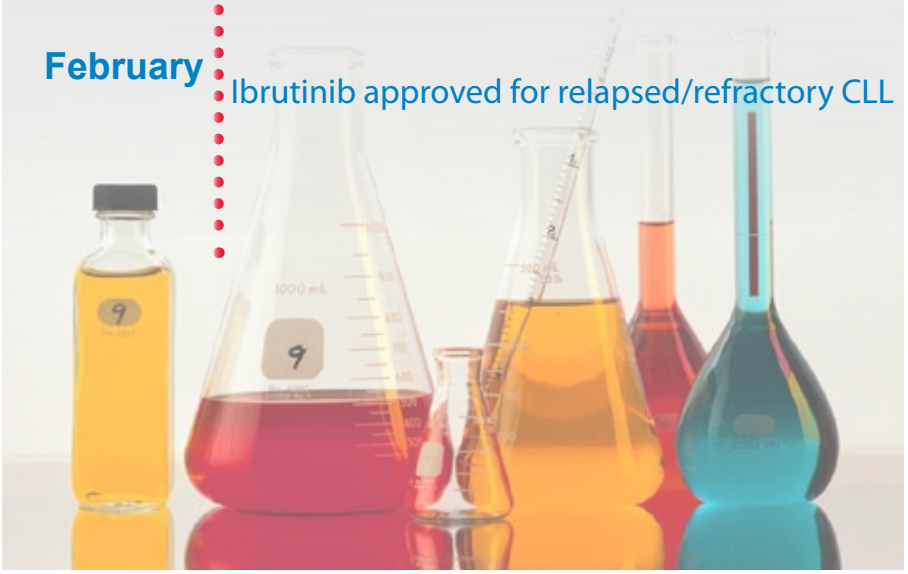
June — Lenalidomide approved for relapsed/refractory MCL

August — Valchlor becomes first FDA approved topical mechlorethamine for CTCL

November — Obinutuzumab and ibrutinib are first Breakthrough Therapies approved by FDA

2014

February — Ibrutinib approved for relapsed/refractory CLL



Professional Education Spring 2014 Programs

Lymphoma ROUNDS Program

Lymphoma Rounds provides a forum for healthcare professionals to meet on a regular basis and address issues specific to the diagnosis and treatment of their lymphoma patients. This program is free for healthcare professionals and available for CME credits.

Los Angeles April 23
Seattle May 1
Chicago May 14
Philadelphia May 14
New England May 21

Caring for the Lymphoma Patient

Caring for the Lymphoma Patient: Managing Patients with T-Cell Lymphoma provides an opportunity for nurses to learn about recent updates on the treatment of T-cell lymphomas and the management of the diseases. This program is free for healthcare professionals; participants will earn four hours of CEU credits.

Chicago May 15

Register at
lymphoma.org/ProfessionalEd

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Lymphoma Research Foundation's

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The Lymphoma Research Foundation's volunteer Scientific Advisory Board, comprised of 45 world-renowned lymphoma experts, guides the Foundation's research activities, seeking out the most innovative and promising lymphoma research projects for support.

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Eighth Annual Boca Luncheon Raises $150,000 for Research

LRF held its Eighth Annual South Florida Luncheon on February 3 at St. Andrews Country Club in Boca Raton. The Luncheon was attended by 300 people and raised nearly $150,000. Since 2007, LRF's Florida Luncheon has raised more than $1.1 million to support its mission.

Boca Luncheon Past and Current Co-Chairs *(L to R): Elisabeth Dalfen, Joan Hauser, 2014 Keynote Speaker Ann S. LaCasce, MD , Mitzi Oreman, Gladys Cook, and Jane Yudell*

"Thanks to the dedication and commitment of our supporters, partners and organizing committee, the Luncheon has become LRF's signature fashion event raising significant funds to support lymphoma research and programs," said Gladys Cook, one of the event's co-chairs.

Guests enjoyed a Fashion Show featuring The ESCADA Spring 2014 Collection presented by Saks Fifth Avenue, Boca Raton and an onsite Saks boutique, where they donated 10 percent of the event sales to LRF. Dr. Ann S. LaCasce, a member of LRF's SAB as well as Assistant Professor of Medicine at Harvard Medical School's Dana Farber Cancer Institute, served as the event's keynote speaker.

LRF would like to thank the Luncheon's past and present Co-Chairs Judith Bronsteen, Gladys Cook, Elisabeth Dalfen, Joan Hauser, Ellen Liebman, Mitzi Oreman and Jane Yudell. Without their hard work and dedication over the past eight years, this luncheon would not have been possible. For more information about the Florida Luncheon, including photos from the event, visit **lymphoma.org/bocaluncheon**. ■

Leave a Legacy

Remember LRF in your will

Your bequest can have a lasting impact on LRF's mission to eradicate lymphoma and serve those touched by this disease.

To learn more about including LRF in your estate plans, please contact us at

plannedgiving@lymphoma.org

Spring 2014 Patient Education Programs

Lymphoma Workshops

Lymphoma Workshops are regional, one-day educational programs that provide the latest information about the diagnosis and treatment of lymphoma, in addition to information about living with a lymphoma diagnosis.

New England (Needham, MA)
March 22

Chicago, IL
May 17

Ask the Doctor

Ask the Doctor About Lymphoma Programs are community-based, two-hour educational programs that provide an update on lymphoma treatment options. This spring, two programs focusing specifically on mantle cell lymphoma (MCL) will be offered.

Bethesda, MD
April 1

Seattle, WA
April 1

Culver City, CA
April 3

Portland, OR (MCL)
May 8

New York, NY (MCL)
June 11

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News from the Field

Diffuse large B-cell lymphoma (DLBCL) patients who test positive for activation of the transcription factor STAT3 may have a poorer response to standard treatments than other DLBCL patients, especially those with the activated B-cell subtype (ABC-DLBCL), suggests a study partially supported by an LRF Career Development Award (CDA). STAT3 activation is a common feature in DLBCL cells with the activated B-cell phenotype. Kai Fu, MD, PhD of the University of Nebraska Medical Center, corresponding author on the study and a 2009 LRF CDA recipient, worked with his team to examine 407 patients for STAT3 activation through archived tissue samples and previously published data. The 37 percent of patients who demonstrated STAT3 activation had poorer overall survival rates and event free survival, particularly those with ABC-DLBCL. The correlation suggests a need for research into alternative treatments that will specifically address DLBCL with STAT3 activation. Source: *Journal of Clinical Oncology*

LRF congratulates Julie Vose, MD, MBA, FASCO of the University of Nebraska Medical Center, on her election as President of the American Society of Clinical Oncology (ASCO). Dr. Vose is an LRF Scientific Advisory Board member and a frequent contributor to other LRF programs, including serving as faculty for the inaugural Clinical Research Mentoring Program. As president of ASCO, Dr. Vose will help lead a professional organization representing more than 30,000 physicians who care for people with cancer. Dr. Vose will take office as President-Elect at the June 2014 annual meeting and serve a one year term beginning in 2015. Source: *ASCO*

The oral drug idelalisib recorded more promising results for indolent non-Hodgkin lymphoma (iNHL) patients in a study published in the March 13, 2014 issue of the New England Journal of Medicine. 125 patients with relapsed or refractory iNHL took part in the study, receiving a twice-daily dose of the drug, which inhibits a family of enzymes known as PI3K deltas, which are found in many B-cell tumors. Following treatment, 57 percent of patients had their tumor size reduced by at least half. 6 percent reported no measurable evidence of cancer. Ajay Gopal, MD of Fred Hutchinson Cancer Research Center in Seattle and a past LRF grantee, was lead author on the study, which is the first publication of clinical data on idelalisib. The drug's promising results in an earlier trial for CLL helped it receive the Breakthrough Therapy designation from the FDA; it is currently awaiting approval for all iNHL. Source: *New England Journal of Medicine* ■