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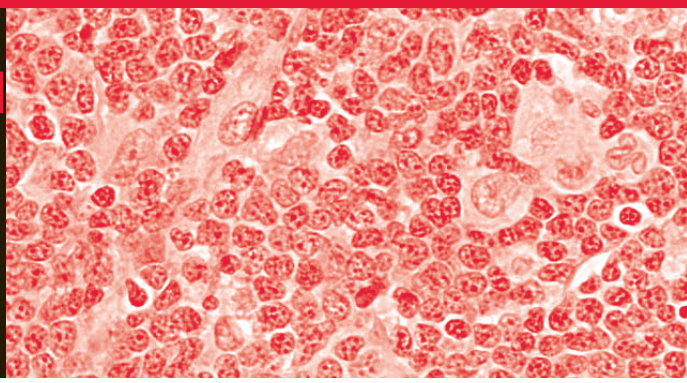
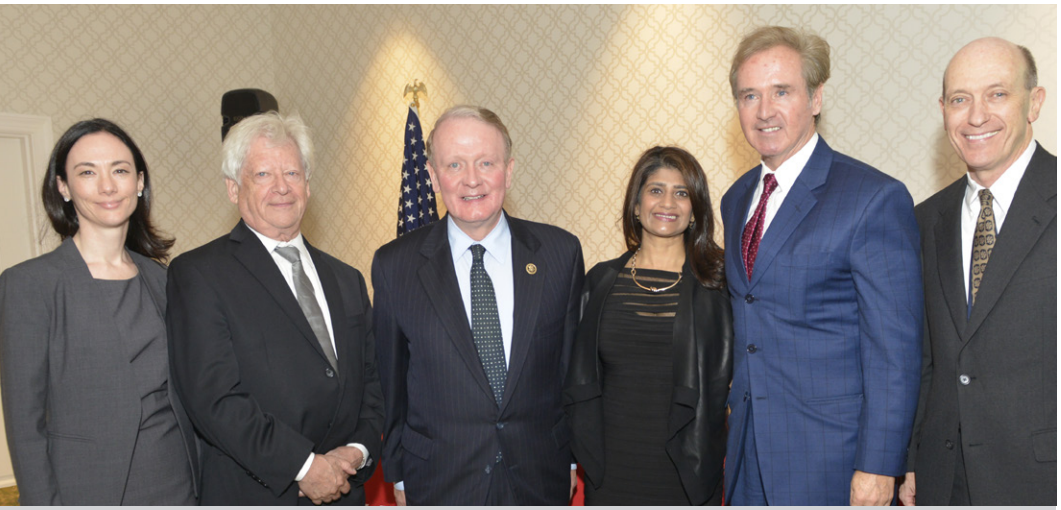
RESEARCH Report



LRF Convenes First-of-Its-Kind Science and Policy Workshop: Oral Therapies in Lymphoma



(L to R) Meghan Gutierrez, LRF Chief Executive Officer, Neil Kay, MD, Mayo Clinic, Rochester, Rep. Leonard Lance (R-NJ), Sonali Smith, MD, University of Chicago, Rep. Brian Higgins (D-NY), and Michael E. Williams, MD, University of Virginia at the Oral Therapies in Lymphoma Workshop.

The Lymphoma Research Foundation (LRF) convened scientists, clinicians, advocates, pharmaceutical industry representatives, and federal lawmakers and regulators this September for a workshop on Oral Therapies in Lymphoma. Lymphoma and chronic lymphocytic leukemia (CLL) are a complex group of malignancies traditionally managed by cytotoxic chemotherapy, immunotherapy, radiation treatment, and, in some cases, by high-dose chemotherapy and stem cell transplantation. Recognizing that cancer care has entered a new era in which targeted oral anti-lymphoma agents are quickly changing treatment paradigms and providing a unique opportunity to improve patient outcomes and survival, LRF hosted the meeting to identify the specific challenges facing the scientific and patient communities related to the development, optimization, treatment adherence, and access to lymphoma oral therapies. The workshop, held in Washington, D.C., engaged and informed key stakeholders of these challenges and the day-long discussion helped to shed light on priority action items for further investigation and investment.

The program began on September 10 with a discussion of access to innovation and the evolving use of oral anti-cancer therapies. Following a brief networking session, Michael E. Williams, MD, ScM, University of Virginia Health System and Cancer Center, LRF Scientific Advisory Board member and workshop co-chair, welcomed attendees and introduced special guests, U.S. Representatives Brian Higgins (D-NY-26) and Leonard Lance (R-NJ-7), authors of the Cancer Drug Coverage Parity Act of 2015 (H.R. 2739), which helps to ensure patient access to oral anti-cancer therapies. The Congressmen spoke about their bipartisan legislation and the importance

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"Up to a quarter and in some cases even half of [lymphoma] patients are being treated with oral therapy... Even three years ago, this would have been far less than ten percent."

- Jonathan W. Friedberg, MD, MMSc

FEATURED IN THIS ISSUE: AYA Lymphoma Research Symposium **Page 3**

LRF's Adolescent/Young Adult Lymphoma Initiative expands its efforts to support AYA-specific research by convening the Foundation's first research symposium devoted to AYA lymphoma biology, treatment, and survivorship issues.

LETTER FROM THE CEO

Dear LRF Friends and Supporters,

Autumn at the Lymphoma Research Foundation is a time of significant activity and advancement. Beginning with Blood Cancer Awareness Month in September, LRF's "Light it Red for Lymphoma" campaign reached more than 2 million social media users and received more than 3 million impressions per week, as patients and survivors used the Foundation's social media tools to educate people about lymphoma and support the Foundation's mission.

The Foundation's Oral Therapies in Lymphoma Workshop, highlighted on the front page of this edition of Research Report, was the first meeting of its kind to discuss issues surrounding the use of this rapidly growing class of therapies. We know the Workshop will have an enduring benefit for individuals living with lymphoma and CLL. The Foundation also convened the first scientific program in our ongoing Adolescent and Young Adult (AYA) Lymphoma Initiative, "Adolescent and Young Adult Lymphomas: Biologic, Therapeutic, and Psychosocial Considerations" this fall. This pivotal symposium assembled pediatric and adult oncologists with AYA expertise to discuss common treatment strategies and identify priority areas for future research to benefit this understudied patient population. A summary of the program is on page 3 and detailed proceedings will be posted on the LRF website in the coming weeks.

The Foundation's premier patient education event, the North American Educational Forum on Lymphoma, welcomed 400 attendees to New York, where they learned about the latest treatment and research advances from the world's leading lymphoma experts. The Forum may have just celebrated its 20th anniversary, but it is still finding new ways to enhance patient and caregiver education. This year, the graduating class of the Lymphoma Clinical Research Mentoring Program was on hand to share their research with Forum attendees (see page 10 for additional details), bringing to life the exciting projects these talented scientists and physicians are pursuing.

Our research and education programs are accelerating at a rapid pace and we are extremely grateful for the dedication, support and contributions of our volunteers and donors. Our thanks to each of you for your part in helping the Foundation impact the lives of those we serve and advance innovative lymphoma research.

Sincerely,

Meghan Gutierrez
Chief Executive Officer

Oral Therapies Meeting

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of ensuring that, as new breakthroughs in treatment are achieved, patients have affordable access to those therapies by assuring that third-party, commercial insurance carriers do not charge patients more in out-of-pocket expenses for oral treatments than for infused or intravenous (IV) therapy.
For many Americans, oral anti-cancer therapies are covered under their health insurance pharmacy benefit while IV treatment is covered under the medical benefit; this differential in payment practice brings with it widely different copayments, coinsurance, and out-of-pocket expenses, often forcing patients to choose between their health and their financial well-being and placing oral therapies out of reach. Patients and providers report numerous advantages and benefits of oral therapies, including improvement of quality of life, greater convenience allowing patients to remain at work and receive treatment close to home, and reduced costs for the healthcare system. Representatives Higgins and Lance highlighted the value of oral therapies, asserted their bipartisan commitment to securing

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LRF Research Symposium Seeks to Identify Priority Research Areas for Adolescent/Young Adult Lymphomas

Eric Lowe, MD of Children's Hospital of the King's Daughters (Norfolk, VA), discusses the pediatric oncology approach to treating anaplastic large cell lymphoma (ALCL).

Lymphomas represent roughly five percent of all new malignancies diagnosed in the United States, but nearly 19 percent of all cancers in 15 to 29 year olds, numbering an estimated 67,000 new diagnoses annually. This population of adolescent/young adults (AYA) face additional challenges in their treatment including delayed diagnosis, a limited understanding of the biology and etiology of the cancers which impact them, and healthcare concerns for survivors such as long-term treatment side effects and secondary cancers.

The Lymphoma Research Foundation's Adolescent/Young Adult Lymphoma Initiative launched in 2014 with patient education programs, awareness campaigns, and the Foundation's first AYA-specific research grant program. On October 2, 2015, LRF expanded the research arm of the Initiative by convening a one-day research symposium Adolescent/Young Adult Lymphomas: Biologic, Therapeutic, and Psychosocial Considerations. "The Lymphoma Research Foundation is committed to supporting the unique needs of adolescent and young adult lymphoma patients," said Meghan Gutierrez, LRF Chief Executive Officer. "The dialogue initiated at the AYA Research Symposium will refine and strengthen the Foundation's ability to support innovative research that directly impacts this patient population."

The AYA Research Symposium assembled an array of experts from across both pediatric and adult oncology to discuss the differences in treatment approaches for the most common AYA lymphomas (diffuse large B-cell lymphoma, Burkitt's lymphoma, Hodgkin lymphoma (HL), and T-cell lymphomas), common biologic features, and survivorship issues including secondary cancers, cardiotoxicity concerns, fertility, and cognitive impact. Attendees sought to share their knowledge with other researchers as well as identify research questions still unanswered.

Symposium attendees included both fellows and early career researchers from institutions across the United States and Canada as well as representatives of several National Cancer Institute (NCI) Cancer Cooperative Groups. "Pediatric and adult oncologists don't often get the opportunity to share research ideas with each other," said Kieron Dunleavy, MD of the NCI, and Co-Chair of LRF's Adolescent/Young Adult Initiative Advisory Committee. "This research symposium was organized around the idea that by working together, we will be better able to identify the most important unanswered questions in treating AYA lymphoma patients, and be better equipped to address those questions in our research."

The program also allowed researchers to consider a variety of issues complicating the treatment and research of AYA lymphomas and identify potential action items, including:

Clinical trial inclusion criteria, including age, complicates treatment plans for patients who turn 18 mid-treatment. Attendees suggested that the creation of institutional programs specifically for 15- to 30-year olds, as well as advocacy efforts for better pediatric/AYA clinical trials, may help address this issue.

Impact of age and differences in drug metabolism and resistance, and the lack of understanding on exactly how these differences impact patient outcomes. Attendees discussed the possibility of conducting a retrospective analysis on trials that included AYA patients to better understand outcomes, biology, and toxicities.

The biology of lymphomas in AYA patients specifically has been understudied compared to older patient populations. For example, Christian Steidl, MD of the British Columbia Cancer Agency, discussed his lab's efforts evaluating the gene expression predictor in pediatric HL, to assess whether or not there are biological differences in AYA lymphoma. (Full results will be presented at this year's Annual Meeting of the American Society

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Oral Therapies Meeting

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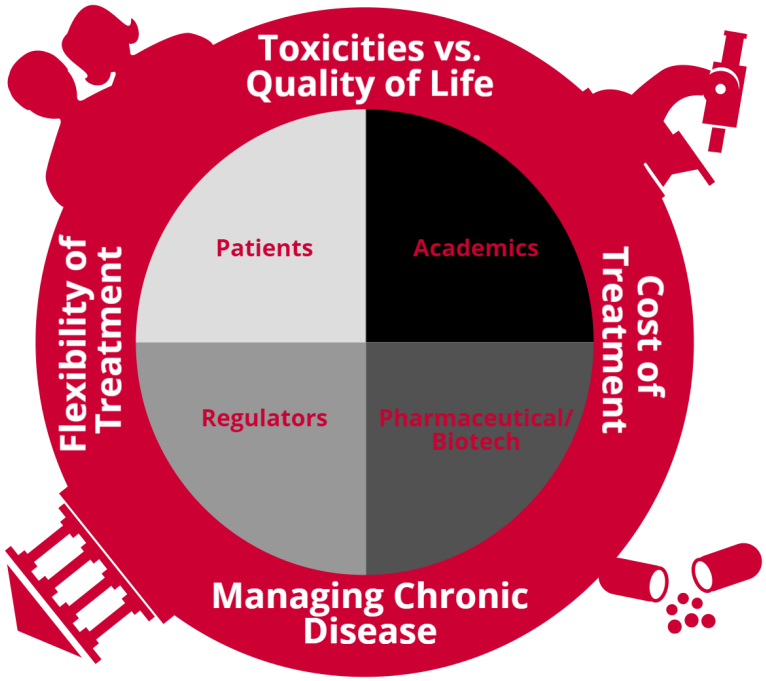
parity in insurance coverage for oral chemotherapy and urged participants to help them build support in Congress for their legislation.

The following morning, workshop co-chairs Jonathan W. Friedberg, MD, MMSc, University of Rochester Medical Center and Dr. Williams welcomed participants. Dr. Friedberg, also a Foundation SAB member, opened the morning session by placing oral anti-cancer drugs in a historical and clinical perspective, referencing recent survey data. "Up to a quarter and in some cases even half of [lymphoma or CLL] patients are being treated with oral therapy. If you had asked this question [of oncologists] even three years ago, I think this would have been far less than ten percent." Dr. Friedberg explained that this "big change in the way that patients are being cared for" and the shift to continuous therapy together lead to a variety of challenges and the need to focus on issues such as compliance, cost, reimbursement, patient teaching and education, measurement of outcomes, endpoints, and natural history of disease.

To ensure a comprehensive exploration of the issues relating to the evolving and dynamic development of new oral therapies for lymphoma and CLL, the workshop program included four main components focusing on key stakeholder perspectives: academic, industry, patient, and regulatory and economic. Each perspective had a panel or presentation portion of the program; highlights of each discussion are provided below.

The Use and Study of Oral Therapies in Lymphoma and CLL: Advancing Diagnostics and Research to Improve Lives

The development and expanded use of novel oral therapies profoundly impacts the future of lymphoma and CLL care. During the first panel, moderated by Dr. Williams, three SAB members discussed the opportunities and challenges with respect to the study and use of oral therapies and identified priority areas for advancing relevant clinical research.



Sonali Smith, MD, The University of Chicago, presented an overview of the prevalence and incidence, clinical applications, and value for oral therapeutics for lymphoma. Dr. Smith discussed the trade-offs and balances that are made by clinicians and patients between efficacy and toxicity. She noted that with some oral drugs being "taken indefinitely," exploration of the "cumulative cost in terms of toxicity, efficacy, and financial burden" must be undertaken. She underscored the importance of adding "value" into the conversation as "the entire discussion [to-date has been on] benefit and toxicity." Dr. Smith also commented on the growing, significant costs and out-of-pocket expenses of oral anti-cancer therapies and the fiscal and moral imperative to "decide as a group how we assign value to a particular agent or combination of agents as we go forward." She noted that part of the value effort is "hampered by the fact that many of the [clinical] trials being done use very weak comparators." Dr. Smith called for more phase III trials and a movement toward "true comparators that are clinically meaningful … so we can truly start to gauge the risk, and the benefit of the different drugs that are out there."

Neil E. Kay, MD, Mayo Clinic College of Medicine, presented on treatment decision points, particularly focused on novel agents for CLL, clinical trial endpoints, and potential adjustments to the structure of clinical trials. Dr. Kay provided an overview of a number of studies relating to CLL treatment, with a focus on chemoimmunotherapy (CIT). He acknowledged that while CIT may not be a "fit" for all patients, he asserted that "in going forward, we're going to still need to compare in our clinical trials CIT against others." Dr. Kay also spoke about the challenges of

some novel therapies with respect to drug resistance, toxicities, and how to manage side effects caused by therapy, such as atrial fibrillation, rashes, diarrhea, and bleeding. He suggested that there needs to be a movement toward the use of surrogate endpoints in future clinical trials that will aid us in making quicker decisions on utility of novel agents- primarily needed "because of the chronicity of the disease." Dr. Kay urged consideration of discontinuation trials to collect better data with respect to how long a novel oral signal inhibitor agent can safely be used for a given patient. This will have needed impact on the durability of response, safety, and cost; he noted that new trials should look at how to best combine novel treatments with the primary goal of helping to "improve on the depth of response with novel agents [to] …and to reach complete remission with minimal residual disease negative status." Dr. Kay also touched on the issue of out-of-pocket expenses for patients, noting that "we have to remember … the annual average household income is around $50K, so this [cost of treatment] gets to be a huge issue for our typical patients."

John P. Leonard, MD, Weill Cornell Medical Center, spoke about the importance of patient monitoring and reporting, particularly as they relate to assessing the burden of toxicities. As part of his presentation, he provided examples of the challenges in collecting valid and reliable, longitudinal toxicities data. Dr. Leonard discussed the importance of focusing the objective of treatment on "feeling better" and urged greater attention to – and improvements in – the monitoring, measurement, and reporting of adverse events, side effects, and quality of life for cancer patients. He specifically underscored

Neil Kay, MD, of Mayo Clinic, asks a question during a panel discussion.

the need to "better understand" what matters to patients and "informing our discussion and decisions that we make in conjunction with patients." Dr. Leonard noted that "our current data collection underestimates these [burden of toxicities] issues" and we "need to work on better defining our goals of therapy." Dr. Leonard also suggested the community move away from progression free survival (PFS) as a clinical trial endpoint, as he does not believe it is a "surrogate for benefit to the patient and feeling better." He asserted that we "need to better characterize these multiple and chronic toxicities," study and better understand compliance, and "look into … chronic versus intermittent therapy." Dr. Leonard acknowledged the challenge of the cost of therapy and suggested there may be non-clinical ways to improve quality of life, such as providing psychosocial support for anxiety and stress, which potentially would boost quality of life for patients and "be more appropriate and less expensive." He challenged the community to prioritize efforts to improve the measurement of quality of life, particularly for indolent lymphomas, and focus on helping the patient "feel better."

All three panelists agreed that cost was a growing concern and the patient was central to expanding understanding of toxicities as well as informing clinical trial design. The group explored the idea of an app, such as the *Focus On Lymphoma* app developed by LRF (see focusonlymphoma.org for more details), or other tools that could help collect toxicity information for patients both in clinical trials and those outside of a trial environment. Panelists also concurred that trials needed to be designed to capture more data to inform discussions about toxicity and value and that real-world, mainstream use of therapies should be examined, longitudinally, outside of the trial setting.

Emerging Scientific Developments: The Pharmaceutical Industry and Regulatory Landscape

The rising number of oral therapies for lymphoma and CLL, both currently marketed and in the development pipeline, will significantly impact most aspects of lymphoma care. This second panel, moderated by Dr. Friedberg, discussed the current state of the science, the patient experience, regulatory landscape, and areas for collaborative research.

Joel Beetsch, PhD, Vice President, Patient Advocacy, Celgene, presented the methodology and findings of a meta-analysis looking at the use of 30-month complete response (CR30) patients with follicular lymphoma. Dr. Beetsch reported that the evaluation found that CR30 could be used appropriately and could "accelerate approval and accelerate the clinical trial process" with "patients [as] winners in this particular case." He also urged support and attention to efforts to

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Since 2006, 24 new therapy designations have received FDA approval for lymphoma/CLL
7 of those approvals have involved an oral therapy
5 of those 7 received the Breakthrough Therapy designation for accelerated approval

Oral Therapies Meeting

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ensure chemotherapy payment parity, noting that 40 states have passed legislation to ensure patient access to oral anti-cancer therapies, and referred to the federal bill Representatives Higgins and Lance have introduced in the House of Representatives.

Danelle F. James, MD, MAS, Head of Oncology, Pharmacyclics, echoed the comments of Dr. Leonard on the importance of having additional endpoints beyond PFS to support physician and patient understanding of effectiveness of therapies. She provided examples of therapies, including B-cell receptor signaling inhibitors with significant clinical benefit but also with other clinical indicators that could have been "considered progression." Dr. James commended LRF for its work to convene experts and issue a white paper that helps to change guidelines for certain agents, such as BTK inhibitors. She underscored the importance of ensuring that while some novel agents may cause an increase in blood lymphocytes, this should not be considered progression or treatment failure a concept which has now been clarified in the CLL guidelines. Dr. James also reported a new efforts needed for oral therapies to "explore the adherence, including the use of concomitant medications, and the side effects that patients are experiencing and the treatment patterns of physicians prescribing." Such phase 4 studies should "inform more broadly on the real world use of the drug."

R. Angelo de Claro, MD, Medical Officer Team Leader, Division of Hematology Products, Office of Hematology and Oncology Products/ Center for Drug Evaluation and Research/ U.S. Food and Drug Administration (FDA), spoke representing his own views and not the official position of the FDA. Dr. de Claro touched on issues related to endpoints, evaluation of clinical benefit, and patient reported outcomes. He made clear that the FDA does not factor cost into its decisions; the Agency primarily evaluates effectiveness and safety.

The panelists together discussed with the workshop participants the need for: new ways to capture patient experience data; more endpoints to describe treatment effect; balancing trade-offs between toxicity, efficacy, and tolerability; educating patients about the importance of sharing their data and experience to inform research efforts; collecting patient reported outcomes; and partnerships between individual companies. The group also explored the growing need to study sequencing of therapies, the combination of targeted agents, the duration and periodicity of treatment, and the issue of salvageability. Participants noted the need to assist patients with care planning, evaluating unmet needs for certain diseases, and improved communication to patients about toxicities and choices in treatment.

The Patient Perspective

This panel, moderated by LRF Chief Executive Officer Meghan Gutierrez, explored the patient perspective as it relates to treatment selection, adherence, financial implications, and care planning. Two patient advocates, Geoffrey Grubbs and Mitchell Orfuss, each spoke about their personal experiences and treatment journeys with their disease. From each of their experiences, having numerous treatment options, participating in clinical trials, using drugs off-label, and generally being able to "borrow treatments from [other] diseases" were central to their quality of life as well as survival. Both Mr. Grubbs and Mr.

Orfuss underscored the importance for each of them of being able to feel "like themselves" and continue to live their lives as uninterrupted as possible; flexible treatment modalities and therapies with lower toxicities played an essential role in their ability to "operate and just be without symptoms." Both of the patients emphasized the high value they placed on symptom-free progression and their thoughts on the importance of efficacy and safety. Neither patient asserted that adherence was a serious challenge for him personally but there was acknowledgment that pills can get missed and that if it can happen to them, then they can understand how other patients can face adherence issues. Meghan Gutierrez noted the theme of the "need to investigate these [oral therapies] and other treatments further," including the importance of studying ways to facilitate "adherence with some of these oral medications" and the ongoing value of monitoring treatment side effects. Both Mr. Grubbs and Ms. Gutierrez highlighted the LRF Focus On Lymphoma app and mentioned its possible utility in supporting patients in medication adherence, tracking quality of life indicators, and supporting patient reported outcomes.

The Economics of Oral Therapies: Cost and Care

This closing session, moderated by Dr. Williams, examined ways in which financial considerations impact patient access and the quality of care, with a particular focus on patients' ability to access and pay for oral anti-cancer medications.

Elena Elkin, PhD, Memorial Sloan Kettering Cancer Center, discussed the numerous considerations taken into account when assessing value for cancer treatment and highlighted the need to learn about overall cost impact and some of the trade-offs within treatment for lymphomas. She noted that cancer is the second most expensive medical condition among adults in the United States. Lymphoma is the third most costly cancer, with spending projected to exceed $15 billion annually by 2020. Dr. Elkin presented information regarding how other countries, such as the United Kingdom and Canada, assess the value and cost-effectiveness of anti-cancer therapies. She noted the value of being able to review these countries' technology appraisals and cost-effectiveness evaluations so we can learn from their "formal and systematic appraisals." She also highlighted the potential of accountable care organizations, medical homes, bundled payments, episode-based payment, and other related models to improve value and reduce cost. Dr. Elkin noted that when providers stand to benefit, or lose, they may be in a better position to encourage high-value care. She underscored the importance of ensuring that patients receive high-value therapies while not bankrupting the system on "care that isn't going to meaningfully improve outcomes" and acknowledged the fundamental tension between the cost of innovation and drug pricing, which is why the discussion must shift to a focus on value. Dr. Elkin also reiterated the themes of the need to conduct longer follow-up of trial patients, realistic comparators, participation in registries, and otherwise undertake longitudinal data collection of toxicities, adherence, outcomes, and healthcare service use. She closed with a call for increasing funding for quality of life, access, survivorship, utilization, and basic, clinical, and health services research.

Workshop Summary

LRF convened the Oral Therapies in Lymphoma Workshop to identify opportunities and potential actions to address challenges related to the development, utilization, and access to oral anti-cancer therapies in addition to treatment adherence. The workshop's panel discussions all presented issues at the intersection of science and policy, which will help inform LRF's patient support, public policy, and scientific activities in the years ahead. Numerous participants noted that many of the issues and recommendations raised over the course of the workshop have relevance not just to oral therapies but to chemotherapy and lymphoma and CLL care generally, including the challenges of toxicities and adherence; the importance of clinical trials; the need to collect longitudinal data, develop surrogate endpoints, and identify better and realistic comparators; and the need to understand, measure, and communicate the value of therapies. Other potential future actions identified include: educating patients on the recruitment, and complexity of, clinical trials; improving patient communication and engagement; increasing patient access to innovative therapies; further incorporating the patient perspective and risk/benefit into research and care; and boosting funding for research.

As a next step, LRF plans to develop a paper to capture and disseminate the workshop's findings and recommendations. "The Lymphoma Research Foundation is proud to bring together diverse groups of stakeholders to discuss the issues surrounding the growing prevalence of oral therapies in lymphoma," said Meghan Gutierrez, Chief Executive Officer. "I look forward to sharing the findings of this pivotal workshop with an even wider audience."

News from the Field: Notable Foundation Publications

LRF grantee Ash A. Alizadeh, MD of Stanford University, published results of his LRF-funded research in the *Proceedings of the National Academy of Sciences* (PNAS) in March 2015. Dr. Alizadeh received a Follicular Lymphoma (FL) Pathways grant in 2012 for a proposal seeking to identify the genetic hierarchy (a set order in which certain genetic mutations occur) in order to better understand how FL develops, and why subgroups of FL differ from each other. The PNAS publication, which is available in full online, describes the researchers' identification of the CREBBP mutation as a key early event that contributes to FL development by suppressing antigen production, and thus keeping the immune system from developing the T-cells that could fight FL tumor cells. These results suggest that the development of therapies targeting CREBBP could be effective across a wide variety of FL subgroups.

Results of the BELIEF trial, which contributed to the approval of belinostat (Belodaq) for relapsed or refractory peripheral T-cell lymphoma (PTCL), were published in the August 10, 2015 issue of the *Journal of Clinical Oncology*. Belinostat, a histone deacetylase (HDAC) inhibitor was approved in late 2014 by the FDA, which cited the BELIEF trial's results in its decision. Patients on the trial received daily 30-minute infusions for five days on a twenty one day cycle; of the 120 evaluable patients, 31 (26 percent) responded to therapy, including 13 complete responses (11 percent). Median response times (length of time without further disease progression) was 13.6 months overall, and better than 29 months for those achieving a complete response. The study, which included LRF Scientific Advisory Board (SAB) member Owen O'Connor, MD, PhD of Columbia University as first author, noted the poor prognosis for PTCL patients and the lack of a standard of care for patients with relapsed or refractory disease, making belinostat's approval an important step forward for this patient group. In September 2015, the study was reviewed by the *New England Journal of Medicine*'s "Journal Watch" blog as a practice changing study.

On August 17, 2015, the U.S. Food and Drug Administration (FDA) approved brentuximab vedotin (Adcetris) for use as a consolidation treatment for patients with classical Hodgkin lymphoma (HL) who have undergone autologous hematopoietic stem cell transplantation. The approval was based on the AETHERA trial, which evaluated 329 patients with classical HL at high risk of relapse post-transplant in a double-blind, randomized study. Researchers on the study, including former LRF Scientific Advisory Board (SAB) member Craig Moskowitz, MD of Memorial Sloan Kettering Cancer Center, found a median progression-free survival rate of 42.9 months compared with 24.1 months in the placebo arm. The trial results were presented at the American Society for Hematology (ASH) 2014 Annual Meeting; further details about this trial may be found in LRF's 2014 ASH Annual meeting coverage at lymphoma.org/researchnews.

Survivors of non-Hodgkin lymphoma (NHL) have an elevated risk for developing melanoma than the general population. A study published online at the *Journal of Clinical Oncology* in August 2015 has for the first time identified two of the risk factors associated with an increased risk of melanoma in NHL survivors 65 years and older. The study, including SAB member Lindsay M. Morton, PhD of the National Cancer Institute as senior author, linked cancer incidence data from the Surveillance, Epidemiology, and End Results (SEER) database with health care claims data from Medicare to look for connections between cancer diagnoses and patient medical history.

Researchers found that chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) survivors were particularly at risk, especially if one of two factors were present – treatment with the chemotherapy fludarabine or who had a history of certain autoimmune conditions such as asthma, Graves' disease, and psoriasis. Patients with one of these risk factors had a two-fold risk of melanoma compared with survivors who did not. The study also found no factors associated with high risk of melanoma among survivors of non-CLL/SLL subtypes of NHL.

Two LRF grantees recently published separate papers describing the previously unknown role of a gene mutation common in the development of diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL). Jiyuan Zhang, PhD, of Columbia University is a 2015 Fellowship grantee whose LRF-funded research seeks to understand the mechanism of the KMT2D (or MLL2) methyltransferase protein, which commonly mutates early in the progression of DLBCL and FL. In the study, published online at *Nature Medicine* in September 2015, Dr. Zhang and his collaborators, including SAB members Laura Pasqualucci, MD and Riccardo Dalla-Favera, MD both also of Columbia,

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News From the Field

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focus on KMT2D's role in DLBCL, discovering that these mutations impair KMT2D's normal functions, which results in increase of germinal center B-cells that can lead to DLBCL.

Dr. Zhang's findings were published simultaneously with those of Hans-Guido Wendel, MD, who recently completed his three-year Follicular Lymphoma Pathways grant, awarded by LRF in 2012. Dr. Wendel's paper, on which SAB member Randy D. Gascoyne, MD of BC Cancer Agency, was a contributor, found similar results by focusing on KMT2D's role in FL, where the gene is one of the most common mutations. The KMT2D gene normally produces a histone modifying enzyme (HME) that turns on a variety of the genes managing B-cell growth and preventing them from becoming malignant. When mutated, these genes are never switched on, causing the proliferation of abnormal B-cells that may become lymphoma. Both sets of researchers further note that these findings indicate that the development of therapies which target KMT2D-deficient cells may be effective for stopping the progression of FL and DLBCL early in its development.

For more research news, visit lymphoma.org/researchnews.

AYA Research Symposium

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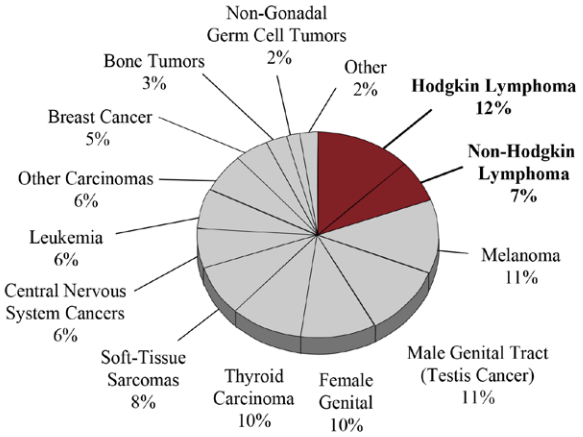
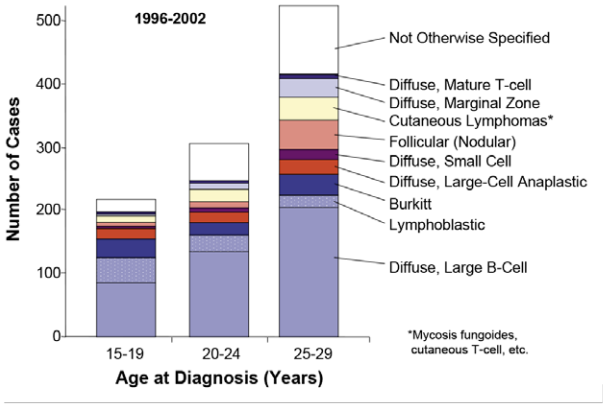
of Hematology in December.) Attendees agreed that projects such as Dr. Steidl's should be undertaken in other common AYA subtypes as well.

"The meeting was an incredible opportunity to meet our pediatric lymphoma colleagues and learn about their approach to treating AYA patients and survivorship issues," said Ann LaCasce, MD of Dana-Farber Cancer Institute, the Committee's other Co-Chair. "The talks on the biology of diffuse large B-cell lymphoma and Hodgkin lymphoma in this age group were also very informative. I have no doubt the meeting will lead to productive future collaborations."

LRF will use the discussion begun at the AYA Research Symposium as a starting point both for addressing AYA issues through the Foundation's research portfolio and to encourage additional collaboration between pediatric and adult oncologists. Tara Henderson, MD, MPH of the University of Chicago and a member of the Symposium's steering committee, believes the Symposium will have an impact in the wider lymphoma research community. "Several significant research questions were raised during the program," Dr. Henderson says, "I'm hopeful that, having identified a few of the questions, we'll be able to begin working towards solutions." Fellow steering committee member Kara Kelly, MD of Columbia University agrees. "This Symposium will help advance the pursuit of AYA specific research not just in the immediate future, but as a long term priority."

Proceedings of the AYA Research Symposium will be published at lymphoma.org/researchnews.





(Top) Incidence of lymphomas among all AYA cancer patients, 1975-2000, (Bottom) Incidence of NHL subtypes in AYA patients 1996-2002.

Source: Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, Including SEER Incidence and Survival: 1975-2000. *National Cancer Institute, NIH Pub. No. 06-5767. Bethesda, MD 2006. Available at http://seer.cancer.gov/publications*

LRF Scholars Represent "Rising Generation" of Researchers at 20th Anniversary Educational Forum

LRF Scholars at the North American Educational Forum on Lymphoma

On October 2-4, 2015, the Lymphoma Research Foundation (LRF) convened the 20th Anniversary North American Educational Forum in Brooklyn, NY. Over the past two decades, the program has provided critical information on treatment options, patient support issues, clinical trials and the latest advances in lymphoma research to thousands of people touched by the disease.

This year's Forum featured a notable first, as the inaugural class of the LRF Lymphoma Clinical Research Mentoring Program (LCRMP) participated in a poster session as part of the Forum's welcome reception. The LRF Scholars, as the program participants are known, presented posters showing the progress of the clinical trials developed through the LCRMP Workshop and made themselves available to discuss their research progress with program attendees. The posters were displayed throughout the weekend, allowing attendees to see first-hand the impact the Foundation is making in the field of lymphoma research.

LRF Scholars began the weekend by attending the AYA Research Symposium (see page 3) and also participated in Saturday's Networking Lunch, visiting with patients in their particular areas of expertise. They also took time to have a follow-up meeting with LCRMP Faculty Co-Chairs and their fellow Scholars, updating the group on their professional and research progress. "This program has been really valuable because of its focus on lymphoma and exclusive size," said Deborah Stephens, DO, of Huntsman Cancer Institute at the University of Utah. "The level of personal attention we all have received is something other mentoring programs cannot match." Fellow Scholar Catherine Lai, MD, of the National Institutes of Health added that she had enjoyed speaking with the patients during the poster session. "As we transition to different phases in our careers, it was insightful to see how other doctors present information to patients. I also really enjoyed my interaction with the patients during the Forum."

Several Scholars have also become involved with other Foundation programs, speaking at Ask the Doctor About Lymphoma patient education programs and Lymphoma Walks, and attending scientific programs relevant to their expertise. Anita Kumar, MD, of Memorial Sloan Kettering Cancer Center, received a 2015 Clinical Investigator Career Development Award, and the program Co-Chairs hope to see more Scholars follow suit in the future.

"I am proud of and impressed with our first class of LRF Scholars," said Kristie Blum, MD of The Ohio State University, founding Chair of the LCRMP Committee. "It has been exciting to witness their professional development over the last two years. I look forward to their continued contributions to the field as both researchers and clinicians." Christopher Flowers, MD of Winship Cancer Center at Emory University and the incoming senior Co-Chair of the Committee, adds "The relationships built through the Lymphoma Clinical Research Mentoring Program, both between Scholars and faculty and among the Scholars themselves, will benefit the entire lymphoma research community by providing the rising generation of researchers with a solid network for mentoring and research collaborations."

2014 LRF Scholars

(L to R as pictured above)

- Jonathon Cohen, MD, MS, Winship Cancer Institute, Emory University
- Deborah Stephens, DO, University of Utah Huntsman Cancer Institute
- Catherine Lai, MD, MPH, National Heart, Lung, and Blood Institute, National Institutes of Health
- Anita Kumar, MD, Memorial Sloan Kettering Cancer Center
- Ryan Cassaday, MD, University of Washington
- Joshua Brody, MD, Icahn School of Medicine at Mount Sinai

SCIENTIFIC ADVISORY BOARD

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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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.

Donor Spotlight

David Delaune of Charleston, South Carolina has donated more than $10,500 to LRF through the workplace giving program of his employer, Boeing. After witnessing his sister's successful treatment for Hodgkin Lymphoma in the early 1990s, David himself was diagnosed with a currently incurable form of non-Hodgkin lymphoma (NHL) in 2002, and discovered LRF's resources through the internet. "I attended multiple 'Ask the Doctor' sessions and the 2002 Educational Forum on Lymphoma," David says. "The information I obtained changed the course of my treatment and I have no doubt I am alive today because of what I learned." David began donating to LRF in order to allow others to benefit from LRF's programs. "Having access to the level of information and resources that LRF provides empowers you and your family," he notes. "I continue to contribute because I want to see all patients empowered with the knowledge on how to fight this disease."

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New Hodgkin Lymphoma Therapy Approved

Consolidation treatment approved by the U.S. Food and Drug Administration

See News from the Field, page 8.

SAVE THE DATE

Update on Lymphoma from the 2015 American Society of Hematology (ASH) Annual Meeting

The Lymphoma Research Foundation invites you to participate in its *Update on Lymphoma* teleconference. This hour-long interactive program will provide an opportunity for members of the lymphoma/CLL community to learn more about the groundbreaking research presented during the ASH meeting, one of the foremost events in hematology/oncology.

Topics will include:
- Overview of Lymphoma
-New Research Presented at ASH
-Disease-Specific Treatment Updates
-The Role of Clinical Trials
-Talking with Your Healthcare Team about Your Treatment Options
-Questions for Our Panel of Experts

Monday, December 14, 2015, 1:30-2:30 pm EST

register at www.cancercare.org/connect or 800-813-4673