Capping off a year that witnessed the treatment landscape in lymphoma expand considerably due to several approvals from the U.S. Food and Drug Administration (FDA), the 2017 Annual Meeting of the American Society for Hematology (ASH) lived up to its reputation as a showcase for the significant strides researchers are making in improving patient outcomes for blood cancers and other hematologic malignancies. Highlights of the 2017 Annual Meeting, held December 9-12 in Atlanta, Georgia, included clinical trials testing promising new therapies, follow-up studies showing sustainable results of the first generation of immunotherapies, new tools for assessing patient prognosis and improved methods for understanding how potential new therapies will translate from the lab to the clinic.

The ASH Annual Meeting has for nearly 60 years been the leading conference for hematologists, oncologists, and researchers across the hematologic malignancies, offering a crucial forum for international discussion of new research and its implications for patient care. More than 20,000 researchers attend the Annual Meeting each year. The Lymphoma Research Foundation (LRF) was well represented at the meeting in presentations and contributions from its grantees, Scientific Advisory Board (SAB) members, and members of its research colloquium and professional education steering committees. Over 480 lymphoma-related abstracts presented at the 2017 Annual Meeting included at least one LRF researcher as an author, with 114 of those researchers serving as the abstract’s presenter -- a role...
Dear LRF Friends and Supporters,

This past December, I had the opportunity to attend the 59th Annual Meeting of the American Society of Hematology (ASH) in Atlanta, Georgia. One of the world’s premier events in hematology, this meeting offers an opportunity for experts in the field to review thousands of scientific abstracts and research papers highlighting critical updates in the study and treatment of lymphoma. This edition of Research Report features a selection of the interesting studies discussed at ASH, many of which featured contributions from Foundation grantees, Scientific Advisory Board members, and scientific leadership.

We often focus on clinical trial results emerging from ASH, but this year’s meeting included significant advances in translational and laboratory-based research, especially involving new tools for predicting patient prognosis and testing new therapies more accurately in the lab. We are proud that LRF-funded research figured in several of these key developments, which are explored in more detail on page two.

In October 2017, LRF hosted a scientific workshop on adherence in oral therapies in lymphoma and CLL. As oral therapies become a standard therapy for many lymphomas, management of this therapy becomes an increasingly critical issue for many clinicians. Please see page eight for a summary of the recommendations from the workshop, which will be released as a white paper in the coming weeks.

This special edition of Research Report allows us to highlight the results of your support for lymphoma research. Thank you for all you do in helping the Foundation advance innovative research and impact the lives of those we exist to serve.

Sincerely,

Meghan Gutierrez
Chief Executive Officer

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generally reserved for a project’s lead or senior researcher. The 45 member LRF Scientific Advisory Board (SAB), a peer-elected group of expert clinicians and scientists in lymphoma who help guide LRF’s research portfolio, saw 93 percent of its members contribute to an abstract, with 58 percent serving as presenters. Meanwhile, 61 percent of LRF grantees who were awarded a grant in the past decade were included on an ASH abstract, with 15 abstracts directly related to LRF-funded research.

“It is always encouraging to see the large number of LRF Scientific Advisory Board members and LRF grantees that participate in the ASH Annual Meeting,” said Thomas M. Habermann, MD of Mayo Clinic, Chair of the LRF Scientific Advisory Board. “This year, to see so many of this group associated with key findings in both clinical and laboratory research speaks to the caliber of scientists that are both steering and contributing to LRF’s investment in cutting-edge lymphoma research.”

Highlights of the Annual Meeting’s clinical research and other studies related to new therapies continue below. Advances in prognostic and laboratory research tools may be found on pg. 2. An overview of epidemiology and clinical endpoints research begins on pg. 10.

New Therapies: Acalabrutinib

An early U.S. Food and Drug Administration (FDA) approval
The 2017 ASH Annual Meeting’s lymphoma research was also a strong meeting for basic and translational science research (research taking place in a laboratory setting and/or involving the transfer of laboratory research to the clinic). Several abstracts presented significant improvements on existing tools for studying lymphoma development in the body, which will help researchers improve both their assessment of existing therapies and their exploration of new ones. As with the clinical developments, LRF grantees and SAB members contributed to many of these developments, including through their LRF-funded research.

An area of significant interest at the 2017 Annual Meeting was circulating tumor DNA (ctDNA), and its potential applications in predicting patient outcomes. When predicting patient outcomes, tumor burden, or the relative mass of the disease present in the body, is a reliable factor for identifying high-risk patients who may need more aggressive treatment. However, current tools for measuring tumor burden are not as precise as researchers would like or require the patient to undergo additional imaging tests. ctDNA consists of DNA from dying tumor cells that is released directly into the bloodstream; because it can be monitored through a high throughput sequencing of a patient’s blood sample, it is a less invasive and, in some cases, less stressful way of measuring a patient’s prognosis.

LRF grantees Ash Alizadeh, MD (also an SAB member) and David Kurtz, MD, both of Stanford University have taken a key role in investigating this topic – Dr. Kurtz’ project for the Lymphoma Clinical Research Mentoring Program (LCRMP) workshop in 2015 was part of the results presented at the Annual Meeting, and Dr. Alizadeh’s Follicular Lymphoma Pathways Grant project was a precursor to the concept of circulating tumor DNA as a prognostic test. At the Annual Meeting, their studies on this topic made up several abstracts, including two presentations delivered by Dr. Kurtz.

The most significant of their presentations was a validation study of ctDNA in diffuse large B-cell lymphoma (DLBCL) – 183 patients from six centers around the world had their blood screened for ctDNA prior to receiving treatment, with 97 percent of patients having detectable ctDNA in their blood. Moreover, Dr. Kurtz and his collaborators found a consistent correlation between the amount of ctDNA detected and the patient’s International Prognostic Index (IPI) risk group, a standardized method for measuring a patient’s prognosis and likelihood of relapse or refractory disease. A similar correlation was found between the amount of ctDNA detected and the amount of time before a patient’s disease progressed after treatment, with higher ctDNA levels correlating with less time before progression. The researchers noted this study verified ctDNA’s use as a prognostic tool and could be used to make more accurate estimates of a patient’s disease burden and refine their treatment appropriately.

Contributors to this study also included MCL Consortium Member Mark Roschewski, MD of National Heart, Lung and Blood Institute, LRF Scholar Jason Westin, MD of MD Anderson Cancer Center, and former SAB member Wyndham Wilson, MD of the National Cancer Institute.

In a session subtitled “New Tools and Emerging Immunomodulatory Approaches for Non-Hodgkin Lymphomas” several abstracts from LRF affiliated researchers examined new methods by which researchers can assess new therapies’ potential in the laboratory before their first in-human tests. Several of the abstracts presented demonstrated construction of patient derived tumor xenograft (PDTX) models in various subtypes.

[CONTINUED ON PAGE 10]
for acalabrutinib (Calquence) in mantle cell lymphoma (MCL) shortly before the Annual Meeting made data on this promising new agent a topic of great interest. Acalabrutinib works by inhibiting the Bruton’s tyrosine kinase (BTK) pathway, a key genetic pathway to the growth of lymphoma cells. Data from the ACE-LY-004 trial, cited by the FDA as being key to their approval, were presented by lead investigator Michael Wang, MD, of the MD Anderson Cancer Center. Dr. Wang, who is a member of LRF’s MCL Consortium, presented data from 124 patients with relapsed/refractory MCL, who took acalabrutinib orally twice daily, until their disease progressed. At a median follow-up of 15.2 months, over half of the patients (56 percent) still remained on the study, with 81 percent of patients exhibiting some response to the therapy. Because of the number of patients still active in the study, a median progression free survival rate and overall survival rate had not yet been reached. Adverse effects of the drug were limited, with only 6 percent of patients discontinuing due to their effects. More significantly, there were no reports of atrial fibrillation (irregular heartbeat), which may indicate an improvement over existing BTK-inhibitors such as ibrutinib, and offer an alternative therapy for patients particularly at risk for that adverse effect.

As with other BTK inhibitors, acalabrutinib is being tested in a variety of B-cell non-Hodgkin lymphomas (NHL), with data from the ACE-CL-003 study showing significant effects for chronic lymphocytic leukemia (CLL) patients. The study, which is in an earlier phase than the MCL study, has treated 19 patients who were receiving their first therapy and 26 relapsed/refractory patients with a combination of oral acalabrutinib and intravenous obinutuzumab. As with the MCL study, most patients (41 of 45, or 91 percent) were still being treated when data was submitted, with 94 percent of relapsed patients and 86 percent of the patients receiving their first therapy having a duration of response of at least 18 months, and only one patient reporting atrial fibrillation, who did not need to discontinue treatment. The investigators on this trial noted that their results indicate this may be an effective new combination for both first line and relapsed CLL patients.

Contributors to this study include LRF grantee Farrukh Awan, MD and former SAB member John Byrd, MD, both of The Ohio State University Comprehensive Cancer Center.

New Combination Therapies: Venetoclax and CLL
Promising news for CLL patients also included results from two trials combining existing therapies with venetoclax (Venclexta), an oral therapy which works by inhibiting the pathway BCL-2. In 2016, venetoclax was approved for CLL patients with 17p deletion who have received at least one prior therapy. Data from the TAP CLARITY trial in the United Kingdom, which administered a combination of venetoclax and ibrutinib for relapsed/refractory CLL patients with and without 17p deletion, reported that all of the 38 evaluable patients on the study experienced at least a partial response – an objective response rate of 100 percent. Furthermore, 32 percent of these patients had no disease following treatment, even when testing for minimal residual disease (MRD) in bone marrow, one of the most sensitive measurements for detecting trace amounts of cancerous cells. Only one patient on the trial experienced tumor lysis syndrome (TLS), a severe adverse effect that has been a concern in some single agent venetoclax trials. This patient was able to pause treatment until the TLS cleared and then resume with no further TLS. Peter Hillmen, MBChB, FRCP, FRCPath, PhD, of the University of Leeds and St. James’s Institute of Oncology in the UK, presented the trial at ASH, and noted in a release that the response rate, number of patients with no minimal residual disease, and lack of increase in toxicity are all encouraging signs of an effective treatment for a population that has not responded to other therapies.

Similar success was reported in a trial of venetoclax and rituximab (Rituxan) in patients with relapsed/refractory CLL. The MURANO trial, a large-scale international trial including contributions from Peter Hillmen, lead investigator on the TAP-CLARITY trial, and former LRF SAB member Thomas J. Kipps, MD of the University of California, San Diego, enrolled 389 patients who had received between one and three prior therapies, and randomized them into two arms. Patients received either rituximab plus bendamustine (a current standard approach for relapsed CLL), or rituximab plus venetoclax. The researchers reported two-year progression free survival rates of 84.9 percent for the 194 patients in the venetoclax arm, vs 36.3 percent in the bendamustine arm, a benefit that extended across both high- and low-risk patients. The researchers further reported an overall response rate of 93.3 percent with venetoclax versus 67.7 percent with bendamustine, indicating that the venetoclax combination was not only effec-
tive for more patients, but prompted a longer response before any disease progression. The MURANO results will be submitted to the FDA in support of converting both the venetoclax/rituximab combination, which received a breakthrough therapy designation in 2016, and the single-agent venetoclax’s accelerated approval into full approval.

Because CLL patients often develop resistance to therapy over time, the promising clinical trial results for venetoclax were accompanied by questions of how to counteract this effect. The results of a laboratory study from the lab of Catherine J. Wu, MD of Dana-Farber Cancer Institute, a prior recipient of an LRF CLL grant, provided early data on a potential resistance-countering strategy. Dr. Wu and her collaborators looked at altered RNA-splicing, a common mutation in CLL cells, and assessed whether combining venetoclax with a splicing modulator, E7107 (or E7), designed to change the RNA-alterations into targets that can be more receptive to venetoclax. In both in vitro and mouse model tests, treatment with E7 and venetoclax resulted in increased effectiveness for the therapy compared to either agent alone, including in a mouse model that appeared initially resistant to venetoclax. The researchers noted that these results indicate that splicing modulators deserve further exploration as a potential strategy to overcome drug resistance and widen the number of patients for whom venetoclax is effective.

> Other contributors to this study included LRF grantees Thomas Kipps, MD of University of California San Diego (also a former SAB member) and Lili Wang, MD, PhD of Beckman Research Institute, City of Hope, as well as Matthew S. Davids, MD, PhD, of Dana-Farber Cancer Institute, a Lymphoma Rounds Steering Committee member.

**New Targeted Therapies: In the Pipeline**

Promising results for new targeted therapies in B-cell NHL were also presented during the 2017 ASH Annual Meeting. A trial spearheaded by two LRF SAB members, Brad S. Kahl, MD of Washington University School of Medicine in Saint Louis – who presented the results – and Owen A. O’Connor, MD of Columbia University Medical Center, reported the first in-human data for loncastuximab tesirine, an antibody drug conjugate, in relapsed/refractory B-cell NHL, primarily diffuse large B-cell lymphoma (DLBCL). Antibody drug conjugates are a class of therapy combining a monoclonal antibody (a type of cell found in the immune system that is able to target specific abnormalities) and a drug designed to kill cancerous cells. Loncastuximab tesirine specifically targets CD19, a biomarker that is often present in B-cell lymphomas. The study recruited relapsed/refractory B-cell NHL patients with aggressive disease who did not respond to other therapies or had no other treatment options. The 68 patients who were evaluable at the time of presentation reported an overall response rate of 60.3 percent, with 35.3 percent experience a complete response. Dr. Kahl noted that nearly all patients experienced some degree of adverse effects, which could be very persistent but which were generally not severe; eight patients (10 percent) discontinued treatment due to side effects. Due to the encouraging number of responses, however, future studies are planned in specific NHL subtypes, including DLBCL.

For patients with cutaneous T-cell lymphoma (CTCL), findings from the MAVORIC study offered new hope for a therapy with a longer lasting response. The randomized trial tested mogamulizumab (Poteligeo), an antibody therapy targeting the receptor protein CCR4, against the standard CTCL therapy vorinostat, for patients with either mycosis fungoides or Sézary syndrome subtypes of CTCL who had failed to respond to at least one prior therapy. Patients in the mogamulizumab arm had a median progression free survival of 6.7 months, compared to 3.8 months in the vorinostat arm – significantly 28 percent of patients responded in some degree to mogamulizumab compared to only 4.8 percent with vorinostat. Because of the disparity in results, patients in the vorinostat arm whose disease progressed or who had severe, intolerable side effects were allowed to cross over to the mogamulizumab arm; 30.1 percent of that group had a response to the new treatment. Based on the results of this trial, the U.S. FDA granted a priority review to mogamulizumab for relapsed/refractory CTCL patients; a decision is expected in mid-2018.

> Contributions to this study included LRF SAB member and grantee Steven M. Horwitz, MD of Memorial Sloan Kettering Cancer, and Lauren Pinter-Brown, MD of University of California, Irvine, Center, a Lymphoma Rounds Steering Committee member.

An international trial of a new Bruton’s tyrosine kinase (BTK) inhibitor, zanubrutinib (also known as BGB-3111), also demonstrated promising clinical activity for a variety of NHL, including significant results in marginal zone lymphoma (MZL). The trial, which was intended to test varying dose levels for safety and efficacy, enrolled 99 patients with NHL subtypes including both aggressive MCL and DLBCL (65 patients) and indolent follicular lymphoma (FL) and MZL (34 patients). In the indolent group, 17 evaluable FL patients had an 18 percent...
complete response rate and 24 percent partial response rate. However, the 26 MZL patients whose data were presented at ASH reported a 78 percent partial response, with no patients seeing their disease progress during treatment.

In the aggressive lymphoma group, DLBCL patients saw results similar to FL, while MCL patients reported a 25 percent complete response and 63 percent partial response. The researchers, including MCL Consortium member Michael Wang, MD of MD Anderson Cancer Center, noted that zanubrutinib, which has in earlier studies reported overall response rates of 90 percent and higher for CLL and Waldenström macroglobulinemia, is still under study in both those subtypes, as well as in a combination study of zanubrutinib and obinutuzumab (Gazyva) in FL, with further studies in the subtypes from this trial planned.

**Immunotherapies Advance Post-FDA Approval**

In October 2017, the FDA approved axicabtagene ciloleucel (Yescarta), a CAR-T cell therapy, for patients with refractory, aggressive NHL based on the findings from the ZUMA-1 trial. Long term follow-up results from that trial were presented, including data from 108 patients (seven from the phase I group and 101 from the phase II group). Researchers reported a median objective response rate (the amount of time a patient experiences a reduction in disease due to treatment) of 11.1 months, and 44 percent of patients had progression free survival of at least 12 months. The median overall survival has not yet been reached for this group. Researchers noted that axicabtagene ciloleucel has proven to be an effective therapy with durable responses for patients who have few other options.

Contributors to this study included LRF SAB member and grantee Nancy Bartlett, MD of Washington University in St. Louis, and grantee John Timmerman of the University of California, Los Angeles.

Another new potential CAR-T therapy for relapsed/refractory DLBCL was presented by Philadelphia Lymphoma Rounds Chair Stephen Schuster, MD of the Abramson Cancer Center, University of Pennsylvania. The JULIET trial tested tisagenlecleucel (Kymriah) in a multicenter international trial which enrolled 147 patients, 81 of whom were evaluable at the time of presentation. The overall response rate was 53.1 percent, with 39.5 percent having a complete response. However, Dr. Schuster pointed out during his presentation that the more significant figure was the response rate at three months (32 percent complete response and six percent partial response) because prior research has demonstrated long-lasting remissions for patients who respond by that point. Tisagenlecleucel received FDA approval in August 2017 for children and adults up to age 25 with acute lymphoblastic leukemia; the JULIET trial data has been submitted in support of an application to expand this approval to adults with relapsed/refractory DLBCL who are ineligible for autologous stem cell transplant.

Other contributors to this study include MCL Consortium member Koen van Besien, MD, PhD of Weill Cornell Medicine, and LRF Scholar Jason R. Westin, MD, of MD Anderson Cancer Center.

Though ZUMA and JULIET are the two trials on which FDA approval for CAR-T are currently based, a number of additional research in CAR-T was presented at ASH, including early clinical studies of CAR-T focused on other pathways than the CD19 pathway targeted by axicabtagene ciloleucel and tisagenlecleucel, and use of CD19 CAR-T in combination with other targeted therapies.

Another class of immunotherapy, checkpoint inhibitors, also saw several notable presentations, including a trial
of a new PD-1 inhibitor, REGEN2810, or cemiplimab. The international multi-center trial treated patients with cemiplimab alone or in combination with REGEN1979, a bispecific T-cell engaging antibody (capable of binding to two different antigens in the cancer cell, in this case CD20 and CD3). The combination therapy arm incorporated B-cell NHL patients, while the monotherapy included both B-NHL and Hodgkin lymphoma (HL) patients. In the monotherapy arm, the B-NHL patients had a complete response rate of 8.3 percent and a partial response of 2.8 percent, while HL patients reported a complete response rate of 26.9 percent and a partial response of 23.1 percent. In the combination arm, which was much smaller, only one of the 12 patients reported a partial response, with 8 patients discontinuing treatment due to disease progression. Researchers noted they are continuing to evaluate the combination therapy with higher REGEN1979 doses, as well as studying cemiplimab as a monotherapy.

Additional contributors to this study include LRF grantee Christiane Pott, MD, PhD of the University of California, Los Angeles, as well as LRF Grantees Echelon-1 is a large international study testing a regimen called A+AVD (brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine) versus the standard frontline therapy ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) in a randomized study. More than 1300 patients were enrolled in one of the two randomized arms. Although the two year progression free survival rate had a small improvement of five percent for A+AVD (82.1 percent) over ABVD (77.2 percent), researchers, including presenter and lead investigator Joseph M Connors, MD of the British Columbia Cancer Agency (a former SAB member), noted that the A+AVD arm had 33 percent fewer patients who needed to receive additional treatment. The investigators noted that these results offer a new, potentially less toxic option for frontline therapy in HL for the first time in nearly 40 years.

Other contributors to this study include LRF SAB Members, Stephen M. Ansell, MD of Mayo Clinic, Nancy L. Bartlett, MD of Washington University in St. Louis, Kerry Savage, MD, MSc of British Columbia Cancer Agency, Anas Younes, MD of Memorial Sloan Kettering Cancer Center, and NY Lymphoma Rounds Steering Committee Chair David Straus, MD, also of Memorial Sloan Kettering.

New Strategies for Existing Therapies

Several significant developments at ASH were presented involving therapies which, though not new to the treatment of lymphoma, were being tested in new patient groups and/or new combinations.

In October 2017, the FDA granted brentuximab vedotin (Adcetris) a breakthrough therapy designation for first-line treatment in classical HL, based on the results of the Echelon-1 study, which were presented at the Annual Meeting’s plenary session, with a simultaneous publication in the New England Journal of Medicine. Echelon-1 is a large international study testing a regimen called A+AVD (brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine) versus the standard frontline therapy ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) in a randomized study. More than 1300 patients were enrolled in one of the two randomized arms. Although the two year progression free survival rate had a small improvement of five percent for A+AVD (82.1 percent) over ABVD (77.2 percent), researchers, including presenter and lead investigator Joseph M Connors, MD of the British Columbia Cancer Agency (a former SAB member), noted that the A+AVD arm had 33 percent fewer patients who needed to receive additional treatment. The investigators noted that these results offer a new, potentially less toxic option for frontline therapy in HL for the first time in nearly 40 years.

Continuing the theme of new treatment options for CLL patients, a trial adding ibrutinib to standard frontline chemo-immunotherapy induced negative minimal residual disease (MRD) status in 83 percent of a group of 35 patients, with thirteen of those patients (37 percent) also achieving a complete response. The trial focused specifically on younger, fit patients (median age of 55) with untreated CLL, a subgroup which had responded well to similar treatment strategies in larger scale trials. Patients
Oral medications are being increasingly used to treat patients with lymphoma and chronic lymphocytic leukemia (CLL). Five oral drugs have been approved over the past three years for eight different indications in lymphoma and CLL. Many patients report numerous advantages of oral therapies, including greater convenience and the ability to receive treatment in close proximity to their home. However, disadvantages such as complex treatment regimens, added caregiver responsibilities for symptom management and financial burden are also reported. As these agents are administered outside of a medical setting, the reasons behind patient nonadherence is difficult to accurately measure, which creates an impediment to the development of related adherence interventions and tools. In October 2017, the Lymphoma Research Foundation (LRF) convened the Adherence and Oral Therapies in Lymphoma and CLL Workshop as a next step identified in the 2015 workshop Oral Therapies in Lymphoma: Opportunities and Challenges in Research and Treatment.

The 2017 workshop was convened with a diverse faculty to explore encourage dialogue among experts in the field on areas of future investigation, including an overview of the epidemiology and types of nonadherence; the need to research polypharmacy (use of multiple drugs simultaneously), adherence and collaborative healthcare models; and the experience of clinicians and researchers working in chronic myeloid leukemia (CML) over the past decade following the introduction of oral tyrosine kinase inhibitors. The workshop co-chairs, Jonathan Friedberg, MD, MMSc, of the University of Rochester Wilmot Cancer Institute and Michael E. Williams, MD, ScM, of the University of Virginia, together with the Workshop Steering Committee – Christopher Flowers, MD, of Emory University, John P. Leonard, MD, of Weill Cornell Medicine and Sonali M. Smith, MD, of The University of Chicago also provided their insights from their work in lymphoma.

Five core themes emerged over the course of the October 2017 workshop:
• Patients on oral therapy regimens generally receive less supervision than those on intravenous therapies and have less interaction with their healthcare team.
• Patients utilizing medications for other health conditions may experience issues including drug-drug interactions, or have additional difficulty adhering to complex regimens or drug administration schedules.
• Currently, there are no standardized methods for assessing, defining, or measuring adherence, and how adherence affects clinical outcomes and disease control in patients with lymphoma is unknown.
• Based on experience with long-term treatment of other malignancies with oral therapies like CML, some side effects may not emerge until after years on the regimen.
• Because of the drug costs and often long duration of treatment required, oral therapies may lead to financial burden or financial toxicity due to high copays. The type of insurance coverage the patient has may be a contributor to poor adherence.

Recommendations included the development of new models of patient management specific to oral therapies; greater patient education about the importance of taking their medication as prescribed; research on the relationship between patients’ level of adherence to oral therapies and disease outcomes in patients with lymphoma and CLL; and the creation of patient registries to capture both short-term and long-term adverse events to capture toxicities that may be bothersome or that may emerge late during treatment.

LRF plans publication of a white paper followed by a proceedings document to help inform decision-making and research within the public, private, and nonprofit sectors. The latter opinion piece will be a call to action emphasizing the need for further research into the impact of adherence and its relationship to patient outcomes.
received ibrutinib along with the fludarabine-cyclophosphamide-rituximab (FCR) chemoimmunotherapy regimen. All 35 patients on the study had at least some response to the therapy, and after a median follow-up of 21 months, no patient died or had disease progression. The results were presented by Matthew S. Davids MD of Dana-Farber Cancer Institute, a member of LRF’s New England Lymphoma Rounds Steering Committee, who indicated that the promising results led to a 50 patient expansion of the trial for further investigation.

Epidemiology and Clinical Endpoints

Clinical research does not always involve the evaluation of new therapies. Several abstracts presented at the ASH Annual Meeting focused on how epidemiological factors such as physical activity, race/ethnicity, and patient finances can impact a patient’s response to therapy and overall outcome. Other types of clinical research analyze compiled data from a number of completed trials to discover important correlations that may help identify high-risk patients before they have a poor response to treatment. The 2017 Annual Meeting featured several abstracts such as these with contributions from LRF grantees and Scientific Advisory Board (SAB) members, offering insights into improving patient care that go beyond response to a given therapeutic agent.

Clinical endpoints – a set period of time in which disease progression commonly occurs – are an important statistic for researchers to validate, as they can help identify a patient’s risk of poor overall survival with standard therapy. In FL, which can exist in both a slow-growing indolent and more aggressive form, developing endpoints that can identify patients with more aggressive disease is particularly important. LRF grantee Carla Casulo, MD, of Wilmot Cancer Institute, University of Rochester, presented a study seeking to validate that progression of disease with 24 months of overall diagnosis (POD24) in FL patients treated with chemotherapy is a marker of poor subsequent overall survival. Using data from 13 clinical trials involving over 5,400 patients, Dr. Casulo and her colleagues, including SAB member Christopher Flowers, MD of Emory University, confirmed POD24 as an early clinical endpoint, as well as identifying other risk factors common to the group that had early progression, such as male gender, high prognostic index risk score, and older age of patients. The researchers noted that POD24 can be used to identify patients eligible for clinical trials designed for high risk FL patients.

A study utilizing data from the Lymphoma SPORE Molecular Epidemiology Resource (MER, a large database tracking lymphoma patients on a number of factors) reviewed the impact of physical activity both before and after diagnosis on the survival of lymphoma patients. Patients in the MER cohort were asked to provide their usual level of mild, moderate, and strenuous physical activity during their adult life prior to diagnosis and then again at their three-year follow up. With over 1300 patients reporting data at both initial and follow up marks, the researchers noted that patients with a higher level of regular physical activity prior to diagnosis had significantly better survival rates; in addition, patients whose physical activity increased at their three-year follow up from their baseline level also had better survival rates than those whose activity was reduced in that time. The researchers, including LRF grantee Jonathon Cohen, MD, MS, SAB member Christopher Flowers, MD, MS (both of Emory University) and SAB Chair Thomas M. Habermann, MD, of Mayo Clinic, noted that the data not only support the importance of physical activity for lymphoma patients, but suggest that a trial of lymphoma patients measuring how increasing physical activity helps their overall survival is warranted.

A study presented by LRF grantee Justine M. Kahn, MD of Columbia University, derived in part from her LRF Lymphoma Clinical Research Mentoring Program project, analyzed data from Children’s Oncology Group trials to seek correlations in survival by race or ethnicity in HL pediatric and adolescent patients. While overall HL survival rates are quite high, some disparities have been noted in populations of blank or Hispanic children and adolescents vs. non-Hispanic white populations. She and her colleagues looked at data from clinical trials conducted by the Children’s Oncology Group; because participants in clinical trials receive comparable therapy and access to care, a disparity in outcomes based on race or ethnicity within these groups may indicate a biological, rather than social, cause underlying the different survival rates. However, after analyzing over 2000 patients on three trials, the researchers found no difference in survival by race/ethnicity within this cohort. Dr. Kahn and her colleagues noted that this suggests the survival gap observed in studies of populations not treated via clinical trial is more closely related to reduced access to
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high-quality care; they plan further analyses to examine treatment related toxicities and secondary cancers by race/ethnicity, as well as the impact of socioeconomic status (independent of race or ethnicity) to outcomes.

Summary
The 2017 ASH Annual Meeting showcased a variety of significant advances in lymphoma research from the laboratory to the clinic, with promising results for new therapies being joined by the exciting potential of circulating tumor DNA and its implications for a less invasive prognostic test (see pg. 2), the first significant change to frontline Hodgkin lymphoma in four decades, and a new understanding of how factors such as patient physical activity and race/ethnicity may impact a patient’s outcome following treatment. Several of these developments were either supported by LRF or involved contributions from LRF Scientific Advisory Board members, research consortium members, and grantees, including several recent recipients of awards for early career researchers and clinicians.

“The Lymphoma Research Foundation is proud to support the development of new therapies for patients” said Meghan Gutierrez, Chief Executive Officer of LRF.

“It is exciting to see so many of our SAB members, grantees, and other colleagues in the research community contribute to advancements in our understanding of the treatment and biology of lymphoma and CLL.”

New Tools
[CONTINUED FROM PAGE 3]

PDTX models, in which tissue from a patient’s tumor are directly implanted into a mouse model, mark an improvement over traditional cell line mouse models because the direct implantation creates an environment for cancerous cell growth that more closely mimics the human body and thus give a more accurate picture of how new compounds may work in human trials. Already at use in many solid tumor and aggressive cancers, the Annual Meeting session looked at recent efforts to create PDTX models for indolent and less aggressive non-Hodgkin lymphoma (NHL) subtypes.

A presentation in this session from senior author and LRF SAB member Andrew Evens, DO, then of Tufts Cancer Center, explained the use of a DLBCL xenograft model, among other tools, to validate a line of natural killer (NK) immune cells for use as a potential CART-cell therapy. A separate abstract detailed a multi-institution project to create a “library” of T-cell NHL PDTX models, in which researchers reported the successful establishment of 41 PDTX models covering a variety of T-cell subtypes including anaplastic large cell lymphoma (ALCL), adult T-cell leukemia/lymphoma (ATLL), and cutaneous T-cell lymphoma (CTCL).

Researchers for the latter study, including SAB members Steven M. Horwitz, MD of Memorial Sloan Kettering Cancer Center and David M. Weinstock, MD of Dana-Farber Cancer Institute, as well as LRF grantees Jia Ruan, MD, PhD and Leandro Cerchietti, MD, both of Weill Cornell Medicine, noted that this library would represent a valuable tool for future studies of potential therapies for T-cell lymphoma patients.

The final presentation of the session featured researchers from Washington University School of Medicine in Saint Louis and research funded in part by an LRF Follicular Lymphoma (FL) Pathways Grant to Todd Fehniger, MD, PhD, who was senior author on the abstract. Noting that personalized tumor vaccines appear promising for FL patients but the process for optimizing the design of these vaccines is not fully understood, Dr. Fehniger and his collaborators tested two new types of genetic sequencing, whole exome sequencing (WES), and RNA sequencing (RNA-Seq), on FL patient samples. Their hypothesis was that data from these processes would help predict patient human leukocyte antigen (HLA) typing (an analysis of a patient’s genetic markers used often to match tissue or organ donors with their recipients) – essentially making it possible to “match” patients with an individualized tumor vaccine. The researchers noted that 30 of the 33 patient samples tested (over 90 percent) expressed genetic markers that are both known to be mutated in FL and from which personalized vaccines can be created, indicating that most FL patients could be treated on clinical trials of these vaccines.

The basic and translational science presented at the ASH Annual Meeting demonstrate that LRF researchers are driving the field forward in the laboratory as well as the clinic by developing new tools and methods for the assessment of patient prognosis and new potential therapies.
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.

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

On February 5, 2018, LRF hosted its Annual Luncheon at St. Andrews Country Club in Boca Raton. More than 270 members of South Florida’s philanthropic community attended the unique fashion event, raising $136,000 in support of LRF.

This year, LRF partnered with Neiman Marcus Boca Raton for a presentation of Spring 2018 trends. Marc Jacobs Beauty served as the event’s luxury cosmetics partner, providing complimentary makeovers and special prizes for attendees. Donna Lennon, a local Boca Raton jewelry designer, hosted a trunk show featuring pieces from her D.A. Lennon Jewelry line, of which 10% of sales were donated back to LRF. The keynote address was delivered by Judy Bronsteen, Gladys Cook, Toby Cooperman, Elisabeth Daffen, Joan Hauser, Gloria Klein, Ellen Lieberman and Mitzi Orenman served as co-chairs of this year’s event.

Since 2007, the Annual Luncheon has raised more than $1.4 million on behalf of the Lymphoma Research Foundation. Judy Bronsteen, Gladys Cook, Toby Cooperman, Elisabeth Daffen, Joan Hauser, Gloria Klein, Ellen Lieberman and Mitzi Orenman served as co-chairs of this year’s event.
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Looking for information on clinical trials?
The Lymphoma Research Foundation (LRF) provides a free Clinical Trials Information Service. LRF’s trained Helpline staff will conduct a search for potential trials based upon information provided by the patient.

Call the Helpline at (800) 500-9976 or email helpline@lymphoma.org

Each year, thousands of Team LRF volunteers across the country turn their talents and interests into impactful support of LRF, doing whatever it takes to make a difference.

WALK WITH LRF: Rally your friends, family and teammates to find a cure for lymphoma at one of our signature events.

RIDE WITH LRF: Cycle through the hills of Maryland with other members of the lymphoma community at our 12th Annual Research Ride, taking place September 23rd. Register today at lymphoma.org/ResearchRide.

RUN WITH LRF: Run in the Rock N’ Roll Marathon series on LRF’s team or run in a marathon of your choice with proceeds benefiting LRF.

FUNDRAISE YOUR WAY: Turn your talents and interests into funds for lymphoma research.

lymphoma.org/TeamLRF