February 2018

Dear Colleague:

To raise awareness of the use of oral therapies in the treatment of lymphoma and chronic lymphocytic leukemia (CLL), the Lymphoma Research Foundation (LRF) convened two national meetings over the past two years, seeking to better understand the role these therapies play in the treatment of cancer and the unique opportunities and challenges presented by the use of oral therapeutic regimens. We were honored to serve as the Co-Chairs of these meetings and to direct this important work.

The first meeting, held in September 2015, convened national experts from a diverse group of stakeholders including scientists, clinicians, policy makers, regulators, drug developers and patients, and produced a set of recommendations outlining areas of future study. These included treatment planning and sequencing, combination therapy and the development of novel targeted therapies. Challenges outlined included adherence, patient monitoring, toxicity management and cost. Chief among these was adherence, an issue which emerged as likely to impact most other areas of drug development and clinical utility. For this reason, LRF’s scientific leadership determined a second meeting focused solely on this important issue was warranted.

In October of 2017 LRF convened the Adherence and Oral Therapies in Lymphoma and CLL Workshop. Through invited presentations and roundtable discussion, the faculty and attendees explored the complexities of patient nonadherence to oral anti-cancer therapy. This white paper has been developed to highlight key discussion items from the Workshop, including the ways in which nonadherence may contribute to poor treatment outcomes and lead to increased health care utilization.

As the Workshop Co-Chairs, we are grateful to the program Steering Committee for their leadership and support in planning this meeting. We also wish to thank the faculty for their many contributions to the Workshop on this important topic. We are appreciative to all who attended and participated in the Workshop, for their interest in exploring these critical themes and discussing ways in which we may ameliorate these issues. Lastly, we are indebted to the LRF staff for their support in developing this meeting.

Motivated by our shared mission to eradicate lymphoma and serve those touched by this disease, we stand with the Lymphoma Research Foundation to address the issues outlined during the Workshop. Through scientific research and enhanced clinical care, we believe we can optimize the use of oral therapies and improve the quality of life for individuals affected by a lymphoma or CLL diagnosis.

Sincerely,

Jonathan Friedberg, MD, MMSc
Michael E. Williams, MD, ScM
Lymphoma is broadly defined as either non-Hodgkin lymphoma (NHL) or Hodgkin lymphoma; chronic lymphocytic leukemia (CLL) is also classified as a type of NHL. In 2016, an estimated 120,440 Americans were projected to be diagnosed with the disease. Many treatment options exist for lymphoma and CLL patients including: chemotherapy, immuno-chemotherapy, immunotherapy, gene and cellular therapy, radiation therapy, stem cell transplantation, and targeted/biologic agents. New agents and combination therapies have been effective in treating many subtypes of lymphoma, a contributing factor to the improvement in survival witnessed over the course of the past two decades.

Currently, several chemotherapy and targeted anticancer drugs that have been approved or are under investigation for the treatment of lymphoma and CLL can be administered orally. Oral agents are demonstrating promising efficacy, albeit with some side effects that are similar to those for anticancer drugs that are administered intravenously. Together, these drugs have ushered in an exciting new era in which targeted anti-lymphoma therapies are changing treatment paradigms and shifting patient expectations regarding their care. Many patients report numerous advantages of oral therapies, including greater convenience and the ability to receive treatment in close proximity to their home. Several challenges regarding the use of oral agents have also become apparent, including patient nonadherence. As these agents are administered independently, patient nonadherence is difficult to assess precisely and numerous barriers exist to accurately measure adherence. The inability to identify the primary cause(s) of nonadherence also creates an impediment to the development of related adherence interventions and tools. While adherence to a therapeutic regimen is essential, the impact of nonadherence in lymphoma and CLL is not well understood and requires further research.

The Adherence and Oral Therapies in Lymphoma and CLL Workshop was convened by the Lymphoma Research Foundation (LRF) to explore these topics in greater detail and encourage dialogue among experts in the field on areas of future investigation. Faculty with professional expertise in these areas provided an overview of the epidemiology and types of nonadherence (unintentional and intentional) as well as the current methods of adherence assessment (e.g., patient self-reporting, prescription refill analysis, biological testing, digital/electronic compliance monitoring) and barriers to accurately measuring adherence that exist. In addition, an expert in the field of chronic myeloid leukemia (CML) delivered an overview of the CML treatment paradigm in the era of targeted oral therapies, relaying the challenges and lessons learned over the past decade in this hematologic disorder following the introduction of oral tyrosine kinase inhibitors. Together, the diverse discussion coupled with a deep understanding of lymphoma etiology and treatment provided a unique forum for synthesizing these issues and formulating a research agenda to address them.
Workshop Agenda

October 19, 2017

8:00 AM  Registration and Breakfast

9:00 AM  Welcome and Workshop Overview
Jonathan W. Friedberg, MD, MMSc
James P. Wilmot Cancer Institute, University of Rochester
Michael E. Williams, MD, ScM
University of Virginia Cancer Center

9:15 AM  Patient Adherence and Oral Anticancer Treatment
Joseph A. Greer, PhD
Massachusetts General Hospital

10:00 AM  Utilization and Adherence of Oral Anticancer Agents: Perspectives and Opportunities from the National Cancer Institute (NCI)
Wendy Nelson, PhD, MPH
Basic Biobehavioral and Psychological Sciences Branch, NCI

10:20 AM  Adherence in the TKI Era, or How to Run the CML Marathon
Michael J. Mauro, MD
Memorial Sloan Kettering Cancer Center

10:45 AM  Break

11:00 AM  Oral Therapies and Adherence in Lymphoma Roundtable Moderate by Drs. Williams and Friedberg
Christopher R. Flowers, MD
Winship Cancer Institute of Emory University
John P. Leonard, MD
Weill Cornell Medical Center
Sonali M. Smith, MD
The University of Chicago

12:15 PM  Summary and Next Steps: Areas and priorities for future investigation
Jonathan W. Friedberg, MD, MMSc
James P. Wilmot Cancer Institute, University of Rochester
Michael E. Williams, MD, ScM
University of Virginia Cancer Center

12:30 PM  Lunch
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. During this period, the Lymphoma Research Foundation Helpline witnessed a 300-percent increase in patient inquiries about oral therapies and as of the date of the Workshop, patients are tracking 23,000 medications in LRF’s mobile app, Focus On Lymphoma. These drugs are perceived as being more convenient for patients and improving their quality of life by avoiding problems that occur with intravenous treatments. Oral medications are also very effective and have improved disease outcomes and patient survival.

Patient use of and adherence to oral medications over long periods of time has also presented challenges, and has not been well studied in patients with lymphoma or CLL. Collaborative efforts between researchers, healthcare providers (for example, physicians, nurses, physician’s assistants, and pharmacists), patient advocates, industry, and government agencies are needed to advance research into the causes and consequences of nonadherence in patients with lymphoma and CLL. Additionally, experiences in other disease states where long-term treatment with oral therapies is prescribed may provide insight and suggest solutions for patients with lymphoma and CLL.

The advent of effective oral therapies has marked a paradigm shift in the way patients receive treatment; however, patient outcomes could be improved with better adherence and monitoring. The LRF Workshop utilized a multidisciplinary approach, which included clinicians and scientists who explored epidemiology, forms of non-adherence, methods of adherence assessment, barriers for accurately measuring adherence, and the clinical implications of non-adherence, to explore the challenges facing the community and possible mechanisms by which these issues may be addressed. Five core themes emerged over the course of the October 2017 workshop:

- Patients prescribed and utilizing oral therapy regimens generally receive less supervision than those on intravenous therapies and have less interaction with their healthcare team. New models for providing care to patients on oral cancer therapies are needed that include increased patient education and more frequent touchpoints.
- Patients utilizing medications to control other comorbidities such as hypertension or diabetes may experience polypharmacy 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 adherence, and there is no uniform definition of adherence nor measure of 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 chronic myeloid leukemia (CML), some side effects may only emerge 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.
New Models for Providing Patient Care

Current patient management protocols for patients with lymphoma and CLL were based on drugs administered by infusion over limited numbers of treatment cycles. New ways of managing patients who take oral medications at home for months or years are needed to improve care and connect patients to their healthcare team.

Patients treated with oral therapies often manage their daily medication use by themselves or with caregivers at home, and have less interaction with and supervision by their healthcare team than do patients treated in a hospital or healthcare facility. When side effects occur, or patients miss a dose of medication, they may often decide for themselves what to do without consulting with their care team.

Patients may ignore or decide to cope with side effects that could be alleviated, leaving them poorly- or under-managed and consequently impacting their adherence to their medication. Prolonged low-level but bothersome side effects may impact adherence more than severe, short-term ones. Therefore, it is important to identify and address all side effects, even those considered mild.

Patients experiencing side effects may become non-adherent for multiple reasons. Patients who experience side effects while taking a medication that is controlling their disease may be reluctant to report the adverse event because they fear that they will be taken off of the drug. When patients miss a dose of medication, they may be uncertain of the impact or how to address the missed dose. Patients may decide to take twice the dose the next day. Alternatively, they may feel that if one dose is working well, two doses will be more effective (over-adherence). Therefore, increased and comprehensive patient education about taking oral medications, what to do when a dose is missed, why over-adherence should be avoided, and reporting treatment-related side effects are warranted to help patients better care for themselves.

While randomized, controlled trials have standardized adverse event reporting criteria, physical symptoms experienced by patients with lymphoma receiving oral medications may be more complex or may not fit into standard adverse event criteria. Side effects may be intermittent occurrences or may appear at different times. Particularly, events that occur later, after several months or years of treatment, may not be recognized as being associated with the oral anti-cancer medication.

Patient perception of some symptoms and how they communicate these symptoms to their care team can also affect how their physician interprets and addresses them; for example, the physician may see these as a new medical condition rather than a side effect of medication. Patients who are anxious about their diagnosis or its treatment may have poorer adherence to oral therapies. Additionally, disease severity or prognosis can affect adherence. Patients may perceive oral medications as being less toxic or less effective than intravenous medications, or may not realize the importance of continuing their oral medication as directed by their physician or attributing adverse effects to the medication.

Patient education and the appropriate provision of that education could address several critical areas of adherence that originate with patient understanding of oral therapy and the goal of their treatment. Nurses may take the lead role in many settings in educating patients about their disease and how to administer oral medications and monitor treatment sides effects. Other resources and staff, such as physician’s assistants, pharmacists, and patient advocacy organizations can also provide relevant information and access to expert patient education materials and resources.

“When you would happen to skip a medication by accident or deliberately did not take a medication, what do you do in those instances? And what kind of education did you receive should you skip a medication? And uniformly patients had no knowledge about how to handle it. People were doing anything and everything from just skipping through to the next day or doubling up on doses to just waiting until they went back to the clinic.”

— Joseph Greer, PhD, Massachusetts General Hospital
Polypharmacy Issues

Polypharmacy is the concurrent use of multiple drugs for one or more conditions and is an underappreciated barrier to oral anti-cancer medication adherence. Potential risks of polypharmacy are drug-drug interactions, drug-food interactions, prescribing cascade, unnecessary treatment changes, and increased healthcare costs. The polypharmacy issue can be particularly burdensome for older patients tracking multiple drug schedules. Other issues that exacerbate this problem are patient cognitive difficulties and use of multiple pharmacies.

These issues underscore the need for a new model for providing patient care. Pharmacists’ access to electronic medical records could offer a way for tracking all the patient’s medications and checking for drug-drug interactions, teaching patients how to take their medications around meals, and suggesting solutions for tracking multiple medications. Mobile apps, such as LRF’s mobile app Focus On Lymphoma that includes medication reminders may be helpful in aiding patients track complex drug schedules or multiple medications. Complex schedules can be further complicated when comorbidities change or an adverse event is misinterpreted as a new medical condition creating prescribing cascades. A holistic approach to patient care may be needed that considers the patient’s comorbidities and other medications in addition to their oral cancer therapies.

Characteristics of Medicare Part D beneficiaries by type of oral cancer medication used

<table>
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<tr>
<th>Characteristic</th>
<th>Imatinib</th>
<th>Erlotinib</th>
<th>Anastrozole</th>
<th>Letrozole</th>
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<tr>
<td>Mean (SD) age</td>
<td>75.3 (6.39)</td>
<td>76.6 (6.6)</td>
<td>75.3 (7.1)</td>
<td>74.8 (7.1)</td>
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<tr>
<td>Mean (SD) number of comorbidities</td>
<td>1.93 (1.93)</td>
<td>3.13 (2.53)</td>
<td>2.04 (1.93)</td>
<td>1.99 (1.97)</td>
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<tr>
<td>Mean (SD) number of noncancer drugs</td>
<td>9.75 (6.63)</td>
<td>13.24 (6.00)</td>
<td>7.71 (4.87)</td>
<td>8.03 (4.99)</td>
</tr>
</tbody>
</table>


Financial Burden

Patient-administered oral anti-cancer medication is routinely covered under a patient’s pharmacy benefit/plan in the United States. As a result of this benefit design, patients are often responsible for proportionally high co-payments when compared to their cost-sharing requirements for anticancer therapies administered in a clinic or hospital setting. Coupled with the overall expenses associated with cancer care and the cost of treatment, abandonment of newly-prescribed oral therapy is not uncommon.

The likelihood of abandonment increases for patients enrolled in health plans with pharmacy benefit designs that require high cost sharing, leading to discontinuation of the therapy because of financial toxicity. Thus, patient insurance status may also be associated with outcomes but has not been studied in this context.
Assessing and Interpreting Adherence

Adherence to a medication regimen is generally defined as the extent to which a person takes medications as prescribed by their physician(s). Measurements such as assessing patients’ plasma drug levels; electronic monitoring of pill counts; pharmacy and insurance records; and self-reporting by the patient, physician, or patient’s family may be tracked. These methods have limitations and biases. Beyond measurement, no consensus exists as to the ideal threshold of adherence and its impact on lymphoma clinical outcomes.

The National Cancer Institute (NCI), a participant in the workshop, has designated adherence to oral cancer therapies as a key research agenda item, offering research grant opportunities in the study of patient characteristics that are associated with adherence; studies on the psychological underpinnings of adherence including how mood disorders may affect adherence; and challenges for adherence in patients with physical limitations or disabilities or those who live in areas where healthcare resources are limited.

In previous studies of adherence, a variety of patient-, clinician-, treatment-, and system-related factors were associated with adherence. Patient factors include patients’ emotional state, health beliefs, social support system, socioeconomic status, and feelings about their disease and its prognosis. Clinicians are challenged to implement the latest therapeutic options in management of a relatively rare cancer. Physician appointment time is short, and developing a physician-patient partnership is challenging, while other healthcare professionals’ time is limited or absent to counsel patients. Treatment factors include the reason for prescribing the therapy, the treatment schedule (simple versus complex regimens), whether a benefit is seen immediately or takes time to achieve, side effects, and costs. System-related factors include patients’ relationship with their healthcare providers and satisfaction with their care, insurance coverage, and the convenience of getting to the clinic where they received their care.

In populations with various types of cancer, the severity of the disease and life expectancy influenced adherence. For example, patients with non-small cell lung cancer, who have a poor prognosis, were more adherent than patients with CML, who have a good prognosis. Complex regimens, particularly those that require patients to take different drugs on different days of the chemotherapy cycle, can also impact adherence.

Drugs may need to be taken with food or on an empty stomach, and some drugs interact with specific foods (for example, grapefruit). When taken in too close proximity to a meal, the drug may be less effective or food can cause increased plasma drug levels and excess toxicity.

When physicians are unaware that the patient is not taking their medication, they may believe that the drug is not effective and unnecessarily change the patient’s drug regimen or, in some cases, increase the drug dose. Additionally, drugs given to treat side effects can have side effects of their own, leading to prescribing cascades, and leaving patients with more medications and treatment-related side effects that they must measure and track.

<table>
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<th></th>
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<td>Ixazomib</td>
<td>Lenalidomide</td>
<td>Lenalidomide</td>
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<tr>
<td>Week 2</td>
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<td>Dexamethasone</td>
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<td>Rest</td>
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<td>Ixazomib</td>
<td>Lenalidomide</td>
<td>Lenalidomide</td>
<td>Lenalidomide</td>
</tr>
</tbody>
</table>

Source: Wendy Nelson, PhD, MPH, National Cancer Institute
Assessing and Interpreting Adherence (cont.)

**Personal Factors**
- Emotional state
- Health benefits
- Social supports
- Feelings about disease, self-efficacy & outcome expectations
- Socioeconomic status

**Treatment Factors**
- Reason for therapy
- Schedule
- Immediacy & evidence of benefit
- Side effects
- Costs

**Interaction With System**
- Relationship with providers
- Satisfaction with care
- Insurance coverage
- Convenience of clinics

Ruddy et al. CA: A Cancer Journal for Clinicians, 2009
Oral treatment of CML may provide a model for oral therapies used to treat patients with lymphoma and CLL. CML oral agents have been available for over 15 years, with an accumulating body of lessons-learned related to adherence. CML can be treated as a chronic condition using daily oral therapy, and treatment may persist for several years or for the patient’s lifetime. There are now several tyrosine kinase inhibitors available to treat CML, and the number of patients living with CML as a chronic condition has increased eight-fold since imatinib first became available.

Good adherence to oral kinase inhibitors is essential to achieve and maintain deep remission in patients with CML. However, patients’ adherence to these drugs tends to decline after about four months, and few patients have greater than 90 percent adherence, a level that is required to ensure ongoing disease control.

The patient may not be aware of the clinical implications of poor adherence and its ultimate impact on disease progression. Poor adherence early in therapy can be related to a side effect, such as skin or gastrointestinal issues. However, longer term side effects, such as cardiovascular events, are emerging and may not be immediately related to adherence and could be mistaken as a new disease. Based on new criteria from the National Comprehensive Cancer Network, some patients with CML who have persistently non-detectable disease may be able to take drug holidays or stop treatment. However, follow up for such patients is very strict and requires close medical monitoring. It is less clear how drug holidays or stopping treatment would benefit patients with lymphoma or CLL receiving oral therapies and these approaches are not recommended currently.

There is a lack of information for patients with lymphoma and CLL regarding the level of adherence that impacts outcomes such as disease control, adverse events, or overall survival. Additionally, information is lacking regarding potential emerging toxicities that may appear after long-term treatment with oral therapies prescribed to patients with lymphoma and CLL. Finally, the potential for stopping therapy temporarily or for extended periods in patients with lymphoma or CLL remains to be determined.

**Chronic Myeloid Leukemia as a Model for Lymphoma and CLL**

**Patient adherence with imatinib therapy estimated at 75%.

Only 41% of patients were more than 90% adherent.

Pharmacy record analysis of patients prescribed imatinib

Tsang, J et al. J Clin Oncol 24, no. 18 suppl (June 2006) Abs 6119

**6-year probability of MMR according to measured adherence rate**

Workshop Findings and Recommendations

To address the core issues highlighted during the Workshop, the faculty and participants suggested several critical areas that require the attention of the lymphoma community and new research investment. It is important to note that many of the recommendations have relevance and applicability for the broader cancer community as well.

**Patient Management and Education**
- Patients require specific instruction regarding therapy administration and required action items should they miss a dose of medication.
- Physicians should ask patients about their level of adherence in a way that does not induce guilt or negatively impact physician-patient communication.
- Mobile applications and other digital tools may provide a way for patients to report symptoms and connect to support systems. Studies suggest that among patients with cancer using a mobile app, patients’ satisfaction with their care and their quality of life improves, and adherence to therapy increases. Mobile apps may particularly help patients who have had poor adherence to therapy in the past or have anxiety about their disease or treatment at baseline.
- Educating patients about their disease, providing instruction on the administration of oral medications, as well as monitoring and reporting of treatment side effects, should be included into their overall management. Roles and responsibilities for educating patients need to be established between nurses, pharmacists, and other members of the patient’s healthcare team.

**Medication Risks and Polypharmacy**
- A single member of a patient’s care team must be responsible for monitoring all medications and supplements being administered and checking for drug-drug interaction. In addition, some member of the care team must be responsible for instructing patients in drug administration and suggesting solutions for tracking multiple medications.
- Access to and regular monitoring of electronic medical records could also offer a way for pharmacists and other providers to assist patients with polypharmacy issues.
- Mobile apps, such as LRF’s mobile app Focus On Lymphoma [www.FocusOnLymphoma.org](http://www.FocusOnLymphoma.org), which includes medication reminders, may be helpful in helping patients track complex drug schedules or multiple medications.
- When an adverse event is misinterpreted as a new medical condition, new drugs may be prescribed for it, creating prescribing cascades. A holistic approach to patient care may be needed that considers the patient’s comorbidities and other medications in addition to their oral cancer therapies.

**Assessing and Interpreting Adherence**
- For patients with lymphoma or CLL, the optimal mechanism to assess adherence needs to be determined.
- The level of adherence or nonadherence to specific drugs that have an impact on outcomes in patients with lymphoma or CLL also needs to be determined.
- Electronic devices such as smart pill bottles that use lights or sound to signal patients when they miss a dose of medication, sends text messages, and includes follow ups from a pharmacist could help remind patients to take a dose of medication.

**Learning From Experience in Other Disease States**
- Like CML, some patients with lymphoma or CLL may be treated long-term with oral therapies.
- Treatment of CML patients with oral kinase inhibitors such as imatinib could provide insights and suggestions for treating patients with lymphoma and CLL. Therefore, literature reviews and cross-disease state forums on the topic of adherence to oral therapy are encouraged.

**Registries to Capture Emerging Toxicities**
- Toxicities, such as cardiovascular events, may not appear until after long-term treatment. Particularly, reporting of events will occur outside of clinical trials where there is no systematic way to gather data.
- In addition to post-marketing studies by pharmaceutical companies, patient registries should be set up to help gather data and to watch for emerging toxicities.
Summary and Next Steps

The Lymphoma Research Foundation hosted the Adherence and Oral Therapies in Lymphoma and CLL Workshop to identify opportunities and actions to address challenges related to patient adherence to oral therapies. The Workshop faculty provided perspectives on the origins and causes of nonadherence, and how information from other cancers treated with oral medications might inform the situation for patients with lymphoma and CLL.

The Lymphoma Research Foundation hopes that this White Paper will inform decision-making within the public, private, and nonprofit sectors, and help prioritize research resource allocation, contribute to improvements in patient care, and facilitate advancements in the study of adherence to oral anti-cancer therapy. In the months ahead, the Foundation will work with stakeholders in the cancer community to pursue the highlighted recommendations and undertake action items identified during the meeting.

For additional information, visit the Lymphoma Research Foundation website, lymphoma.org.
APPENDIX

Workshop Co-Chairs

Jonathan W. Friedberg, MD, MMSc, is Director of the James P. Wilmot Cancer Institute, and Samuel Durand Professor of Medicine and Oncology. He is a driving force behind the operations of our clinical programs research aspects of the Wilmot Cancer Center. Dr. Friedberg serves as chair of the lymphoma committee in SWOG as part of the National Clinical Trials Network, and has served as principal investigator on many local and national lymphoma treatment protocols for both Hodgkin lymphoma and non-Hodgkin’s lymphoma.

Dr. Friedberg received his medical degree from Harvard Medical School. His postgraduate training included an internship and residency at Massachusetts General Hospital. He also completed a medical oncology and hematology fellowship at Dana-Farber/Partners Cancer Care in Boston.

Dr. Friedberg also has an M.M.Sc. degree from Harvard Medical School in clinical investigation. His research interests focus on development of novel therapies for patients with lymphoma. He was awarded the Scholar in Clinical Research award from the Leukemia & Lymphoma Society, based upon his work with an oral inhibitor of a protein called Syk, which demonstrated efficacy in the treatment of several different forms of lymphoma, and chaired the Education Program of the American Society of Hematology annual meeting last year. He also serves as Associate Editor for hematological malignancies for Journal of Clinical Oncology.

Michael E. Williams, MD, ScM, is the Byrd S. Leavell Professor of Medicine and Professor of Pathology; Chief, Hematology/Oncology Division; Director, Hematologic Malignancies Program at the University of Virginia Health System, Charlottesville.

Dr. Williams received his MD from the University of Cincinnati College of Medicine and a Master of Science from the Harvard School of Public Health. He completed his Medicine residency, Chief Residency, and Fellowship in Hematology/Oncology at the University of Virginia Health System in Charlottesville, where he currently serves as Chief of the Hematology/Oncology Division.

Dr. Williams’ research interests are in novel therapeutic approaches for non-Hodgkin lymphoma and CLL, including targeted agents and immuno-therapeutics. He serves on the Scientific Advisory Board and the Executive Committee of the Lymphoma Research Foundation, is a member of the European Mantle Cell Lymphoma Network, and is Vice-Chair of the Eastern Cooperative Oncology Group Lymphoma Core Committee.

Dr. Williams is past Chair of the Hematology Subspecialty Board of the American Board of Internal Medicine. He participates regularly in national and international programs devoted to education and research in lymphoma and CLL.
Workshop Steering Committee Members

Christopher R. Flowers, MD, is a Seattle native; he completed his undergraduate and medical training in California. He graduated from Stanford University from the Human Biology and Humanities honors programs. He remained at Stanford where he completed medical school and a master's degree in Medical Information Sciences. After medical school, he returned to Seattle where he completed internal medicine residency at the University of Washington. After residency, Dr. Flowers continued his research spans training in Seattle through the Robert Wood Johnson Clinical Scholars Program and oncology fellowship at the Fred Hutchinson Cancer Research Center. At the University of Washington, he collaborated on studies that investigated the cost effectiveness of pharmacogenomics in oncology, and developed clinical and translation studies in chronic lymphocytic leukemia and non-Hodgkin’s lymphoma.

Dr. Flowers currently serves as Professor of Hematology and Oncology at Winship Cancer Institute at the Emory University School of Medicine. He additionally serves as Clinical Director for Oncology Informatics Program, and is a member of the Emory Stem Cell and Bone Marrow Transplant team as well as directs the lymphoma clinic at Emory. His current research span three areas: 1) translational research clinical trials in non-Hodgkin’s Lymphoma, 2) oncology informatics projects developing an information infrastructure to support pharmacogenomics and outcomes research, and 3) medical decision analyses and cost-effectiveness analyses aimed at developing strategies to individualize care for cancer patients.

Neil E. Kay, MD’s laboratory research is focused on B-chronic lymphocytic leukemia (CLL). This most common and still incurable leukemia is not fully understood in terms of both its clinical and biologic heterogeneity. However, because it is both a frequently diagnosed leukemia and provides ready access to leukemic cells, it proves to be an ideal tumor model for a variety of in vitro studies.

To support the laboratory studies described below, Dr. Kay and his colleagues have established an extensive CLL tissue bank and clinical database that is a rich, nationally recognized resource for CLL studies.

Dr. Kay’s work involves close collaboration with several other talented scientists at Mayo Clinic, including Diane F. Jelinek, Ph.D., in the Department of Immunology; Curtis A. Hanson, M.D., and Daniel L. Van Dyke, Ph.D., in the Department of Laboratory Medicine and Pathology; James R. Cerhan, M.D., Ph.D., in the Division of Epidemiology; and Susan L. Slager, Ph.D., in the Division of Biomedical Statistics and Informatics. This collaboration has provided for unique studies in CLL that now include extramurally funded studies in CLL B-cell signaling, detailed epidemiological studies of CLL and genome-wide analysis of familial CLL patients (CLL families with two or more CLL patients). Dr. Kay is also very involved in the design and implementation of CLL clinical trials for previously untreated and treated CLL patients that incorporate the latest novel drugs alone or in combinations. These trials are conducted within the national cooperative group system of the United States.
John P. Leonard, MD, is the Richard T. Silver Distinguished Professor of Hematology and Medical Oncology and Associate Dean for Clinical Research at the Weill Cornell Medical College. He is Vice Chairman for Clinical Research of the Department of Medicine and Associate Director of the Cancer Center at Weill Cornell Medical College and New York Presbyterian Hospital, where he also serves as Attending Physician, Chief of the Lymphoma Service and Director of the Joint Clinical Trials Office in New York City. He received his medical degree from the University of Virginia School of Medicine in Charlottesville, and completed his residency in medicine at New York Hospital–Cornell Medical Center and Memorial Sloan-Kettering Cancer Center.

Dr. Leonard completed a fellowship in hematology and oncology at Cornell, and served as chief medical resident at New York Hospital–Cornell Medical Center. His primary research interest is in the development of novel therapeutic strategies for the treatment of lymphoma and related hematologic malignancies. Much of his work has involved the development of novel therapies for lymphoma, including monoclonal antibodies, other immune-based treatments, targeted agents, and other innovative approaches.

Dr. Leonard’s research has been published in numerous medical journals, and he has served as a member of the editorial boards of Blood and Journal of Clinical Oncology, leading international journals in these fields. He is Chair of the Lymphoma Committee of the Alliance for Clinical Trials in Oncology, a multicenter cooperative group and key component of the National Cancer Institute’s National Clinical Trials Network. Dr. Leonard is an elected member of the American Board of Internal Medicine and American Society of Clinical Investigation.

Sonali M. Smith, MD, is a Professor in the Department of Medicine at The University of Chicago, and Director of the Lymphoma Program. Her clinical research interest is in the development of new agents and rational combinations in the management of both treatment-naïve and rel/ref lymphomas. She has a special interest in the prognosis and biology of lymphoma, with an ultimate aim to personalize approaches based on individual risk factors. Dr. Smith has a number of leadership positions with national and international visibility. She is Vice-Chair of the SWOG Lymphoma Committee where she oversees clinical trial development at the cooperative group level and mentors faculty across the country.

She is the incoming chair of the Continuous Professional Development Committee for ASCO and currently serves as the chair of the ASCO Women in Oncology Subcommittee, and is also scientific track leader for Lymphoma/CLL for 2017. She has been an active member of ASH and is currently co-editor of Hematology, the society’s annual education book. Her previous ASH service includes membership on the Committee on Communications (2003-2007), the 50th Anniversary Planning Committee (2005-2007), the Committee on Education (2011-2014), representation to the American College of Radiology, faculty at the inaugural Clinical Research Training Institute in Latin America (2014), speaker at the Highlights of ASH and other small ASH meetings, and many years of providing abstract review and session moderator. She is also co-chair of the CIBMTR Lymphoma Working Group, and is currently studying the role of stem cell transplantation for patients with high-risk follicular lymphoma. She has a special passion for patient education and is on the Scientific Advisory Board for the Lymphoma Research Foundation where she is also involved in mentoring junior faculty dedicated to lymphoma, and recently co-chaired the 2017 Lymphoma Clinical Research Mentoring Program and chairs the LRF Chicago Rounds. Through ASH, ASCO, CIBMTR, LRF and SWOG, Dr. Smith collaborates on research projects, provides physician education, and works on workshops and websites aimed at providing reliable information for patients and families affected by lymphoma. She has over 130 publications and given almost 200 presentations to peers and/or patient audiences. She is also on the Editorial Board of JCO and Cancer. In July 2017, she became the Elwood V. Jensen Professor of Medicine in the Section of Hematology/Oncology.
Speaker Biographies

**Joseph Greer, PhD** is the Program Director of the Center for Psychiatric Oncology & Behavioral Sciences and the Associate Director of the Cancer Outcomes Research Program at the Massachusetts General Hospital Cancer Center. He is also an Assistant Professor of Psychology at Harvard Medical School.

Dr. Greer's research focuses on the development and testing of supportive care interventions for patients with cancer. As the principal investigator and collaborator on numerous grant-funded projects, he is studying the application of cognitive-behavioral therapy (CBT) to treat anxiety in patients with advanced cancer; the use of mobile technology to promote symptom management and adherence to oral chemotherapy medications; and the benefits of early palliative care integrated with standard oncology care.

Dr. Greer has published over 80 scholarly papers, reviews, chapters, and commentaries related to this work. He has received funding from the National Institutes of Health, American Cancer Society, Patient Centered Outcomes Research Institute, and philanthropic donations. Dr. Greer's program of research is greatly informed by his clinical practice at the MGH Cancer Center where he provides CBT for patients and their families.

**Michael J. Mauro, MD** is Professor of Medicine, leader of the Myeloproliferative Neoplasms Program, and clinical director of the Leukemia Service at Memorial Sloan Kettering Cancer Center in New York City. After receiving his BS and MD from Dartmouth College and Dartmouth Medical School in New Hampshire, he completed both residency and fellowship training at the New York-Presbyterian Hospital/Weill Cornell Medical College in Manhattan. Before joining Memorial Sloan Kettering, Dr. Mauro was on the faculty of Oregon Health and Sciences University for 13 years, where he directed the CML clinical trial program and was involved in the early development and sentinel clinical studies of ABL kinase inhibitors for CML. Dr. Mauro's clinical expertise is in treating patients with chronic myeloid leukemia (CML) as well as other myeloproliferative disorders, including myelofibrosis, polycythemia, and thrombocytosis as well as less common conditions such as eosinophilic and mast cell disorders.

He holds positions on the boards of the International CML Foundation, the MAX Foundation, and the Leukemia and Lymphoma Society.

**Wendy Nelson, PhD, MPH** has been a program director in the Behavioral Research Program at the National Cancer Institute, National Institutes of Health, since 1999. She received her undergraduate degrees from Smith College and Duke University School of Nursing, her MPH from Johns Hopkins School of Hygiene and Public Health, and her PhD in clinical psychology from Saint Louis University. Dr. Nelson completed a clinical psychology internship at Harvard University Medical School and a postdoctoral fellowship at Northwestern University Medical School. Prior to her career in psychology, Dr. Nelson was an oncology nurse at Memorial Sloan-Kettering Cancer Center and a Nurse Officer in the U.S. Public Health Service.

Her public health career included an Epidemic Intelligence Service fellowship with the Centers for Disease Control and Prevention, and several years as an epidemiologist in the Center for Drug Evaluation and Research at the Food and Drug Administration. Before coming to NIH, Dr. Nelson was assistant professor in the Department of Psychiatry and Behavioral Sciences at Northwestern University Medical School. At NCI, Dr. Nelson developed the Basic and Applied Decision Making in Cancer Control initiative in an effort to bridge basic judgment and decision-making science and applied cancer prevention and control research. Her research interests include medical decision making, the role of numeracy in health-related decision making, cognitive effects of cancer and cancer treatment, adherence to oral anticancer agents, ethics of clinical trials, and human subjects research protections.
Glossary

Adherence: taking medication as prescribed with regard to daily amount, dosage, and frequency

Adverse reaction: a side effect caused by a drug or therapy

Chemotherapy regimen: combinations of anti-cancer drugs given at a certain dose in a specific sequence according to a strict schedule

Comorbidities: conditions not related to the cancer

Drug-drug interaction: the pharmacological or clinical response to the administration or co-exposure of a drug with another drug that modifies the patient’s response to either or both drugs

Financial toxicity: problems a patient has related to the cost of medical care. These problems may include a lack of health insurance or having mounting costs for medical care which may lead to debt and bankruptcy.

Over-adherence: non-adherence to a dosing regimen where an increased dose is taken by the patient. Overuse may affect therapeutic efficacy with the potential for increased toxicity.

Patient monitoring: measurement of adherence patterns which includes administration of a drug and side effects

Polypharmacy: the simultaneous use of multiple drugs by a single patient, for one or more conditions

Prescribing cascade: administration of a new drug to a patient because of side effects produced by another drug. Later drugs increase the risk of further side effects, drug interactions, and patient harm. A prescribing cascade usually results from the failure of the health care prescriber to recognize a patient’s presenting disease as evidence of an adverse drug reaction.

Regimen: A specific combination of drugs (chemotherapy), their doses and their schedules of administration. A regimen may also include radiotherapy.

Toxicities: unwanted side effects of cancer therapies, such as decrease in blood cells, nausea and vomiting, and hair loss.

Specialty pharmacy: the service created to manage the handling and service requirements of specialty pharmaceuticals, including dispensing, distribution, reimbursement, case management, and other services specific to patients with rare and/or chronic diseases.
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