Patients Against Lymphoma

Non-Profit | Independent | Evidence-based

Founded in 2002

EIN: 51-0426732

A plea for support for our mission and project to advance the routine and informed consideration of clinical trials

xxx

xxx

xxx

xxx

Dear xxx:

Lymphoma is a blood cell cancer that afflicts about 700,000 American citizens, killing approximately 200,000 people globally each year.[1] There are approximately 50 types of lymphoma – some that are managed conservatively with lower toxic therapy as needed; other types have a rapid fatal clinical course if not cured.

Cure rates for lymphoma vary significantly by type. Hodgkin's lymphoma affecting younger patients has a high cure rate. Here the need is to reduce the toxicity of therapy while maintaining and improving the cure rate – therapies that can lead to late occurring health problems such as second malignancy.

For the most common type of aggressive non-Hodgkin's lymphoma cure is common but a sizable proportion are not cured with initial therapy – requiring high risk salvage therapy with stem cell rescue that helps a small percentage of such patients – those who have chemotherapy-sensitive disease.

A small minority of patients with advanced indolent lymphomas may be cured with standard therapy. Estimates and opinions vary because relapses can be delayed – can occur well beyond five years. Indolent lymphoma can require many treatments over the course of the disease – prompting the question: is it feasible to routinely cure indolent lymphoma with initial treatment? Increasing the urgency to evaluate novel management and curative approaches is the ongoing risk of transformation to an aggressive behavior and treatment resistance over time.

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[1] Jemal A. Global burden of cancer: opportunities for prevention. Lancet. 2012;380 (9856):1797–9 [PubMed]

3774 Buckwampum Road, Riegelsville PA 18077
Tel: 610-346-8419 Fax: 801-409-5736 Email: Support@Lymphomation.org

We are Patients Against Lymphoma (PAL), a non-profit organization founded in 2002 by caregivers and survivors of lymphoma. With the help of our scientific advisors, we provide the online patient community with evidence-based education and resources on lymphoma and its treatments – which includes debunking untested claims for alternative medicine and raising awareness of clinical trials and background on emerging study drugs.

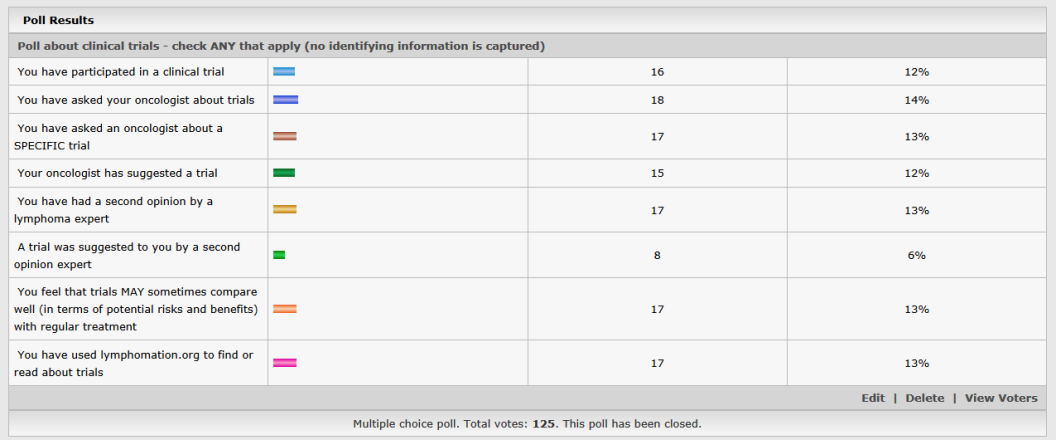
We also moderate and participate in support forums that provide an opportunity for patients and caregivers to ask for or give help to other patients and caregivers. The usage of our website is significant with many thousands of patients and caregivers making use of our educational material and clinical trial location tools.

An independent host server: 35,000 to 128,000 UNIQUE visitors per month, 2010-2013.

Where we are in the consideration, participation, and enthusiasm for clinical trials in the patient community

Patients with online access do not seem to share investigator and advocates enthusiasm for clinical trials

In a recent online survey, the percentage of patients asked to consider trials and who look favorably on trials as a potential treatment decision was lower than expected – lower than a previous finding.[2]



Poll Results

Poll about clinical trials - check ANY that apply (no identifying information is captured)

You have participated in a clinical trial	16	12%
You have asked your oncologist about trials	18	14%
You have asked an oncologist about a SPECIFIC trial	17	13%
Your oncologist has suggested a trial	15	12%
You have had a second opinion by a lymphoma expert	17	13%
A trial was suggested to you by a second opinion expert	8	6%
You feel that trials MAY sometimes compare well (in terms of potential risks and benefits) with regular treatment	17	13%
You have used lymphomation.org to find or read about trials	17	13%

Edit | Delete | View Voters

Multiple choice poll. Total votes: **125**. This poll has been closed.

We are in the process of getting additional feedback from the community to help identify obstacles to enrollment in appropriate trials.

[2] Schwartz, K. Interest, attitudes, and participation in clinical trials among lymphoma patients with online access , JCO, 2009 Journal of Clinical Oncology

Education

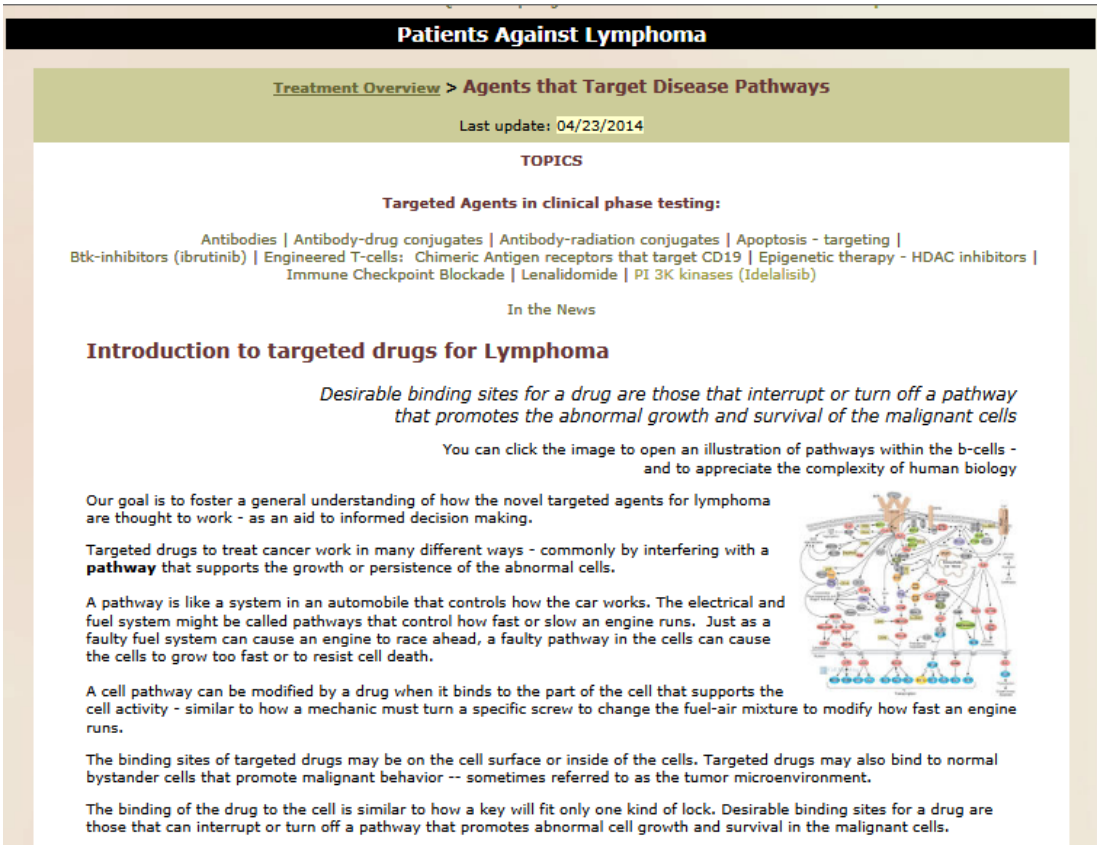
Standard approaches can be effective but also have significant limitations, toxicities and risks. There are numerous investigational targeted agents for the treatment of lymphoma, arising from insights into the disease biology; however, bringing these new agents into regular practice is held back by the slow accrual in clinical trials – the growing number of studies competing often for the same participants in a limited pool of patients asked to consider and willing to participate in trials.

ClinicalTrials.gov, June 26, 2014: 1,454 studies found for Open Studies | Lymphoma OR CLL

So these are the best and worst of times … having unprecedented potential to more effectively treat lymphoma with less toxicity, with no corresponding advances in our clinical trial system – where it's uncommon for patients to be asked to consider a clinical trial.

So a focus of our group is on education about the disease and its treatments – with a focus on helping patients to become more informed about emerging scientific opportunities to test new approaches in clinical trials.

Example: background on study drugs



Patients Against Lymphoma

Treatment Overview > **Agents that Target Disease Pathways**

Last update: 04/23/2014

TOPICS

Targeted Agents in clinical phase testing:

Antibodies | Antibody-drug conjugates | Antibody-radiation conjugates | Apoptosis - targeting | Btk-inhibitors (ibrutinib) | Engineered T-cells: Chimeric Antigen receptors that target CD19 | Epigenetic therapy - HDAC inhibitors | Immune Checkpoint Blockade | Lenalidomide | PI 3K kinases (Idelalisib)

In the News

Introduction to targeted drugs for Lymphoma

Desirable binding sites for a drug are those that interrupt or turn off a pathway that promotes the abnormal growth and survival of the malignant cells

You can click the image to open an illustration of pathways within the b-cells - and to appreciate the complexity of human biology

Our goal is to foster a general understanding of how the novel targeted agents for lymphoma are thought to work - as an aid to informed decision making.

Targeted drugs to treat cancer work in many different ways - commonly by interfering with a **pathway** that supports the growth or persistence of the abnormal cells.

A pathway is like a system in an automobile that controls how the car works. The electrical and fuel system might be called pathways that control how fast or slow an engine runs. Just as a faulty fuel system can cause an engine to race ahead, a faulty pathway in the cells can cause the cells to grow too fast or to resist cell death.

A cell pathway can be modified by a drug when it binds to the part of the cell that supports the cell activity - similar to how a mechanic must turn a specific screw to change the fuel-air mixture to modify how fast an engine runs.

The binding sites of targeted drugs may be on the cell surface or inside of the cells. Targeted drugs may also bind to normal bystander cells that promote malignant behavior -- sometimes referred to as the tumor microenvironment.

The binding of the drug to the cell is similar to how a key will fit only one kind of lock. Desirable binding sites for a drug are those that can interrupt or turn off a pathway that promotes abnormal cell growth and survival in the malignant cells.

3774 Buckwampum Road, Riegelsville PA 18077
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We also help patients to think about the clinical circumstances where participating in a trial should be considered routinely, such as when the lymphoma becomes resistant to standard therapy or when the risk of relapse is high for a protocol with curative intent.

CONSIDERING CLINICAL TRIALS based on your unique clinical circumstances

http://www.lymphomation.org/clinical-questions.PDF

QUESTIONS THAT CAN BE ANSWERED ONLY BY CLINICAL TRIALS

http://www.lymphomation.org/clinical-questions.PDF

QUESTIONS THAT CAN BE ANSWERED ONLY BY CLINICAL TRIALS

A. Which new treatment is effective when standard treatments are not?

Because cancer cells can develop resistance (become refractory) to standard treatment, there's an urgent need to answer this question by testing new agents that target cancer cells in new ways.

Patients with refractory cancer urgently need such studies to be completed, and may also benefit early by participating in dose-finding (phase I and II) safety studies.

B. Which therapy is best as first therapy?

For patients there might be no more important clinical question to answer, because our first therapy is generally considered the best opportunity to cure or improve our survival.

As with Question C, patient participation in trials is required to answer this critical question.

D. Can this new treatment cure a cancer that is not yet cured with standard treatments?

Patients will of course identify with this research objective, but we must also inquire about the potential increased risks that may emerge from any new approach, and how we will be monitored for safety.

E. Can this new treatment manage my condition better than observation?

With the emergence of targeted therapies there's an increased potential to manage indolent cancers by treating as needed, perhaps regularly with less toxic protocols.

However, if the net effects of the intervention are modest, studies may require a control group and random selection to objectively measure and compare benefits and risks. Here's an exception in oncology where a placebo control *might* be required.

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Helping patients, caregivers, and oncologists to locating trials in different ways

Our web-based tools are designed to help the community and treating physicians to locate clinical trials for lymphoma in various ways in multiple venues:

1) Through our website on pages dedicated to understanding and locating clinical trials

2) By posts made to our support forums, and

3) By notices made to social media – facebook and twitter.

We assume that individuals will look for trials for different reasons and in different ways. So we have developed 3 main ways to find trials:

1. Following a favorable published report, by searching for open trials by the type of study drug.

2. When first diagnosis or relapsed, an appropriate study might be located by searching for trials by the type of lymphoma and the patient's treatment status in order to narrow the range of the search.

3. By reviewing what we call PAL's Picks – Trials of Interest. These are studies that look promising to our group and by our scientific advisors based on recent reports. These are listed in order to foster the conversation about trials with the patient's oncologist or by consulting an expert for a second opinion.

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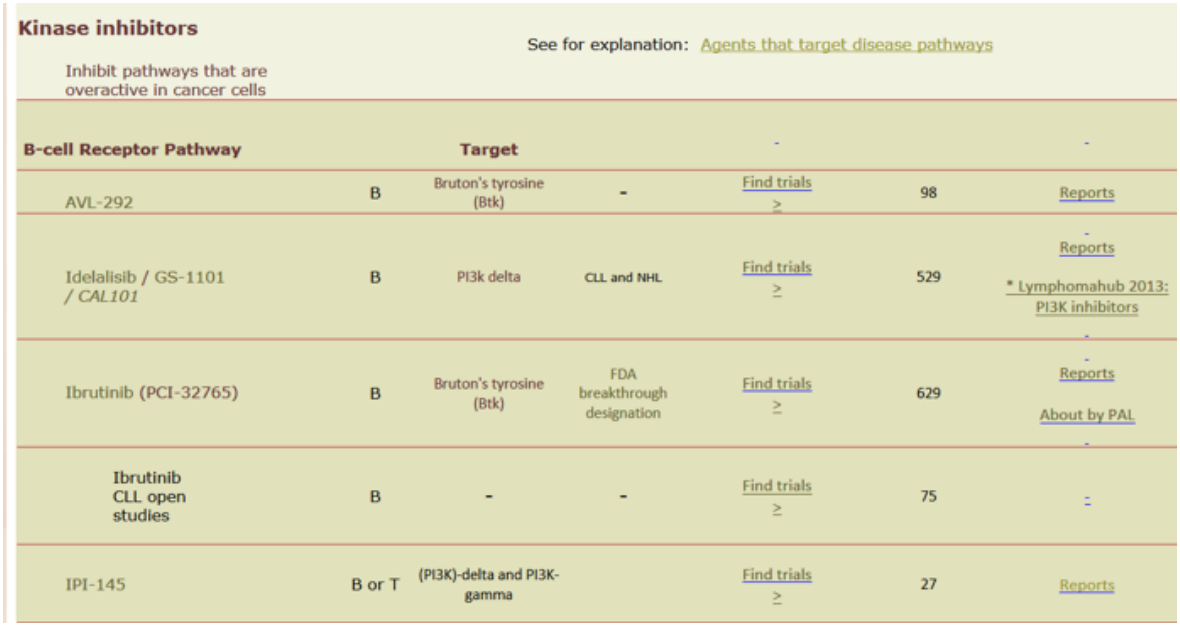
Example: **Locating trials by agent**

From the top of this page the visitor can

- Find trials by the Class or type of agent –
- Or by agents of special interests based on recent encouraging clinical reports

Example: Locating trials by agent - kinase inhibitors



Kinase inhibitors

Inhibit pathways that are overactive in cancer cells

See for explanation: Agents that target disease pathways

B-cell Receptor Pathway		Target				
AVL-292	B	Bruton's tyrosine (Btk)	-	Find trials ≥	98	Reports
Idelalisib / GS-1101 / *CAL101*	B	PI3k delta	CLL and NHL	Find trials ≥	529	Reports * Lymphomahub 2013: PI3K inhibitors
Ibrutinib (PCI-32765)	B	Bruton's tyrosine (Btk)	FDA breakthrough designation	Find trials ≥	629	Reports About by PAL
Ibrutinib CLL open studies	B	-	-	Find trials ≥	75	-
IPI-145	B or T	(PI3K)-delta and PI3K-gamma		Find trials ≥	27	Reports

From this page the visitor can find trials based on the study drug name:

- Click name of agent to list articles on Google scholar that describe how the drug is thought to work (its mechanism of action).
- Click Find trials to list files for this agent in the ClinicalTrials.gov registry.
- Click the ≥ symbol to see latest click count by bitley.
- Click Reports to list published outcome reports on the agent on Google Scholar

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Example: PAL's Picks – Clinical Trials of Interest

Patients Against Lymphoma

PAL's picks - Clinical Trials of Interest

For physicians, patients, and caregivers - an aid in the discussion of trials.

CLL/SLL | CNS Lymphoma | DLBCL | Follicular | Hodgkin | Mantle Cell | Marginal Zone (MALT) | T-cell Lymphomas | GVHD

Mixed types of lymphoma in same trial | New Trials of Interest

Last update: 06/13/2014

See also Lymphoma type & treatment status | Type of Agent | Agents targeting disease pathways

↔ *indicates potential to change practice*

New trials of interest

* Expanded Access
Idelalisib in Combination With Rituximab in CLL http://1.usa.gov/1kKOkMC

Chronic Lymphocytic Leukemia and Small Lymphocytic Leukemia (CLL/SLL)

See also lymphoma - mixed, aggressive, and indolent

CLL/SLL Relapsed or Refractory with 17p Deletion

Testing: ABT-199 an inhibitor of BCL-2

Locations: Tucson, Arizona and Harvey, Illinois

Study drug reports

Clicks as of 6/13/14: 35 Today: >

CLL / SLL relapsed OR previously untreated, OR no prior transplant

Testing: ABT-199 WITH Rituxan

Location: Multiple centers in many regions of US and abroad

Study drug reports

Clicks as of 6/13/14: 136 Today: >

CLL / SLL relapsed < 36 months after last treatment with current need to treat

Comparing: Idelalisib With Bendamustine VS Rituxan VS Bendamustine and Rituxan ↔

Location: Numerous centers in many regions of US and abroad

Study drug reports

Clicks as of 4/27/14: 37 Today: >

CLL / SLL relapsed or refractory

From this page the visitor can review our picks of studies of interest as a discussion aid.

- Find trials by Type of lymphoma and key eligibility

  For each type of lymphoma the protocols are listed in study drug order
- Find studies open to patients with different types of lymphoma, by clicking Lymphoma – mixed, indolent and aggressive
- See the number of centers at a glance
- Find reports on Google Scholar by clicking Study drug reports
- Click the > symbol to see latest click count by bitley
- Estimate the interest level in the study by the number of clicks
- Identify studies with the potential to change practice ↔ Symbol

Example: Find by type of lymphoma and treatment status

Find Trials By Type of Lymphoma and Treatment Status

Last update: 06/13/2014

Also find trials by Agent | PAL's Picks: Trials of Interest See also Related Resources | About Counts

HIV-related | ALCL | Burkitt's | CNS | Childhood | CLL/SLL | Cutaneous | DLBCL PMBCL | EBV-related | Follicular | Hodgkin's lymphoblastic | MCL | MZL / MALT | Ocular | PMBCL | T-cell | Transformed | Waldenstrom's | Other: QOL, GVHD, MDS, CIP-Neuropathy

Type of Lymphoma Click count as of Feb 2013: 3,861 *TIP: From ClinicalTrials.gov, click On a Map to locate trials by region*	Previously Untreated	Clicks since 9/16/13 2,027	Relapsed	Clicks since 9/21/13 1,295	Relapsed AND Not Transplant	Clicks	Other (by request)
AIDS/HIV-related 6/11/14	Untreated	≥ 11	Relapsed	≥ 13	Not Transplant	≥ 10	Relapsed & transplant ≥ 10 Return
Anaplastic Large Cell 6/11/14	Untreated	≥ 21	Relapsed	≥ 24	Not Transplant	≥ 14	Return
Burkitt's 6/11/14	Untreated	≥ 34	Relapsed	≥ 29	Not Transplant	≥ 20	Return
Central Nervous System 6/11/14	Untreated	≥ 75	Relapsed	≥ 58	Not Transplant	≥ 17	Return
Childhood (rare) 6/11/14	Untreated	≥ 8	Relapsed	≥ 6	Not Transplant	≥ 14	Return
Chronic Lymphocytic Leukemia (CLL/SLL) 6/11/14	Untreated	≥ 515	Relapsed	≥ 180	Not Transplant	≥ 39	Return
Cutaneous (skin) lymphoma 6/11/14	Untreated	≥ 22	Relapsed	≥ 18	Not Transplant	≥ 18	Return
Diffuse Large B-Cell (DLBCL) revised display when opened (R) 6/12/14	Untreated	≥ R ≥ 202	Relapsed	≥ R ≥ 231	Not Transplant Transplant	≥ 155 ≥ 15	Autologous Transplant ≥ 43
DLBCL, Alliance Trials 6/11/14	All Studies	≥ 33	-	-	-		Return
Primary Mediastinal B-cell 6/11/14	Untreated	> 60	Relapsed	> 53	Not Transplant	≥ 20	Return

From this page the visitor can:

- Click the type of lymphoma for background on it, such as its natural history.
- Click Untreated or Relapsed to list studies in the ClinicalTrials.gov registry based on the diagnosis and treatment status.
- Click the ≥ symbol to see latest click count by bitley.
- Click Reports (further left and not seen) to list published outcome reports on the agent on Google Scholar

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Please help

We are writing to request a donation of $4,000 (a suggested amount) to help to support our mission:

> Helping patients to become informed participants in their care while advancing the routine and informed consideration of clinical trials for lymphoma, such as by providing tools to:
>
> - Locate trials (and reports) by type of treatment agent
> - Locate trials by type of lymphoma and treatment status

In this request for support we will focus on describing the resources we have developed that expand awareness of investigational choices for physicians and their patients – making clinical trials easier to find and consider.

Our mission is unique

For patients and caregivers to participate meaningfully in medical decisions – including the consideration of clinical trials - requires having a basic understanding of the natural history of the disease (its anticipated clinical course) and having an awareness of the efficacy and limitations of available therapies – specific to ones clinical circumstance and the type of lymphoma.

The purpose of the content and explanations we provide on our website, lymphomation.org, is to help patients to become better consumers of medical information – helping patients to become critical thinkers who can then ask more informed questions of their medical providers.

Additionally, the extensive survivorship topics that we cover are based on patient and caregiver questions.

Importantly, PAL helps to meet the information needs of patients in recognition of the significant psychosocial impacts of the disease and treatments – the emotional stress of a diagnosis, or relapse, the overwhelming sense of isolation and loss of control over one's life; and first-hand knowledge that misinformation is widespread on the Internet, and patients are vulnerable and prone to predatory quackery.

In this era of information overload, the incredibly shrinking medical appointment, and the emergence of the e-patient movement, being well-versed in the methods [of interpreting data] is no longer optional (Zilberberg, MD).

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Guided by our scientific advisors, we provide newly diagnosed patients with information from the most credible sources such as NCCN.org, CllinicalTrials.gov, and Cancer.gov.

Clinical research - a poverty of riches

The potential to make additional progress against lymphoma is increasing dramatically because of insights into the biology of the disease and advances in the development of new agents -- evident by the high number of new agents under clinical investigation for lymphoma.

But the *challenge* of getting the studies done is also increasing – substantially.

For example, we calculated that there were about 24 lymphoma patients available per study at an estimated enrollment rate of 5%, which suggests that enrollment could be **six times** as challenging for lymphoma compared to breast cancer.

See for more detail on this analysis:
http://www.lymphomation.org/lymphoma-enrollment.pdf

While substantial progress has been made against many types of lymphoma, current therapies often fail patients, leading to substantial pain, suffering, and untimely death from the disease or from the side effects of therapy.

"The biggest problem [for lymphoma] is not a lack of new agents or identification of molecular targets. The biggest challenge is enrolling patients in a timely manner on clinically meaningful trials,"
Dr. Annas Younes, Oncology Times, February 2011

Your gift will enable us to continue to build, improve, and maintain the clinical trial tools we provide for a diverse range of lymphomas, already utilized by patients, loved ones, and treating physicians.

PAL's Find Trials by Type of Agent – with click counts

PAL is guided by our board of directors, the published peer-reviewed medical literature, our scientific advisors, and our public policy advisors and advocates.

We are supported entirely by public donations and do not accept donations from companies that provide health services or products – which makes it particularly challenging for our group to meet expenses.

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Organizational accomplishments and partnerships

PAL provides seven moderated support forums with over 2,500 subscribers (2/09)

Independent AWSTATS reports show an average of over 105,000 unique visitors and over 1,500,000 hits (January-April 2011).

We have presented a Teleconference for Nurses and Social workers sponsored by Lance Armstrong Foundation, Leukemia and Lymphoma Society in July 2009.

Our President and Co-Founder, Karl Schwartz, authored a study titled "Interest, Attitudes, and Participation in Clinical Trials among Lymphoma Patients with Online Access" which was published in ASCO 2009. [3]

Karl has been a participant in several FDA Advisory Committee meetings; serves as a patient advocate in the Alliance cooperative group; is a returning member of the faculty for the AACR/ASCO 2012 Methods in Clinical Cancer Research; and is a new member of the Stand Up to Cancer Joint Scientific Advisory Committee and the NCI Lymphoma Steering Committee.

PAL is also a member of The Lymphoma Coalition, a global network of not-for-profit lymphoma patient organizations sharing a vision to free the world of lymphomas - now with a membership of 53 organizations from 38 countries.

Board of Directors:

PALs board members have direct experience with the disease as patients or caregivers and are experienced and dedicated patient navigators – providing support online or at home to afflicted patients and families.

Jama Beasley also moderates a lymphoma support group with an interest in immune therapies, in particular vaccines.

Linda Gerstley, PhD., also provides information and guidance to patients on the Webmagic forum.

Carol Lee also moderates a lymphoma support group for patients and caregivers fighting Marginal Zone lymphomas – nhl-MALT@yahoogroups.com

[3] Schwartz, advisors, JCO / ASCO 2009, Interest, attitudes, and participation in clinical trials among lymphoma patients with online access

Dennis McComb also provides support for two family members who are survivors of different types of lymphoma.

Use of Funds:

Your donation will be used to pay expenses, and to compensate authors, editors and others who contribute to the development of the clinical trial tools -- and related educational content:

1) Website development and management
2) ClinicalTrials.gov query design and testing
3) Writing and distribution of notices about trials, trial location tools and related background information, such as outcome reports for investigational agents.
4) Writing and editing of topics related to lymphoma and its treatment
5) Responding to questions by support forum members or website visitors
6) Survey design, editing, distribution and analysis

PAL Budget:

Our 2011 IRS filing shows that we operate with a very small budget – expenses last year of only $21,400:
http://www.lymphomation.org/PAL%20f990ez-2011.pdf
and that we operated at a significant deficit last year.

Based on usage statistics – such as bitly click counts, PAL is already achieving many of its goals!

We are seeking financial support in order to sustain and improve on the services we provide.

Goals & Objectives & Measures:

Our objectives are as follows:

1. To provide evidence-based background about lymphoma in plain language
2. To describe in plain language how investigational therapies differ from regular therapies -
3. To increase awareness and understanding of the purpose of clinical trials and when they might be considered
4. To provide guidance on how patients might discuss clinical trials with their treating oncologists

5. To encourage consultation with independent lymphoma experts about clinical trials

6. To increase community and physician usage of our single-click clinical trial location tools.

Measuring success as we move forward

1. We will develop and provide online surveys to discover if the educational content and tools provided by PAL have increased in use by the patient and caregiver community (community); and have achieved the objectives described within.

2. We will publish the results of surveys in order to reinforce the objectives provided above and to identify gaps in understanding about clinical trials and how to routinely consider participation.

3. We will continue to make use of bitly.com reports - to measure how often our queries and direct links to trials are used by the community. (See attached example).

Evidence that we are achieving our goals:

Find trials by type of lymphoma and treatment status:

3,680 clicks as of February 2013

Find trials by type of treatment agent

4,651 as of March 2013

We thank you in advance for reviewing our request for support.

We would be happy to answer any follow-up questions that you may have and to provide details of our services to patients and how we measure the effects of our work.

"Improved treatments for cancer will be delayed and patient lives will be lost unnecessarily unless the efficiency and effectiveness of the clinical trials system improves."
(Institute of Medicine)

Sincerely,

Karl Schwartz
President, Patients Against Lymphoma

Attachment: *Letter of Support – By Doctor Maurice Bendandi, MD, PhD*
Screen captures: examples of two clinical trial location tool

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