

Patients Against Lymphoma



Non-Profit | Independent | Evidence-based

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Founded in 2002

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RE: Adding clinical-setting search fields to the ClinicalTrials.gov registry

TO: Staff at prsinfo@clinicaltrials.gov

Dear Sir or Madam:

First, we congratulate and thank you for developing and providing ClinicalTrials.gov, a vital publicly accessible registry of clinical trials for life-threatening conditions. Its importance is borne out by use statistics, approximately **20 million page views per month!**

Our group is among the users of this vital registry, and part of our daily activity is to monitor and review studies that may be of interest to patients with lymphomas.

See <http://www.lymphomation.org/clinical-trials-gov.htm> or Appendix below.

During a recent presentation we learned that patients and patient surrogates are the primary users of ClinicalTrials.gov, as shown in Figure 1, almost certainly for the purpose of locating clinical trials that may help address urgent clinical needs.

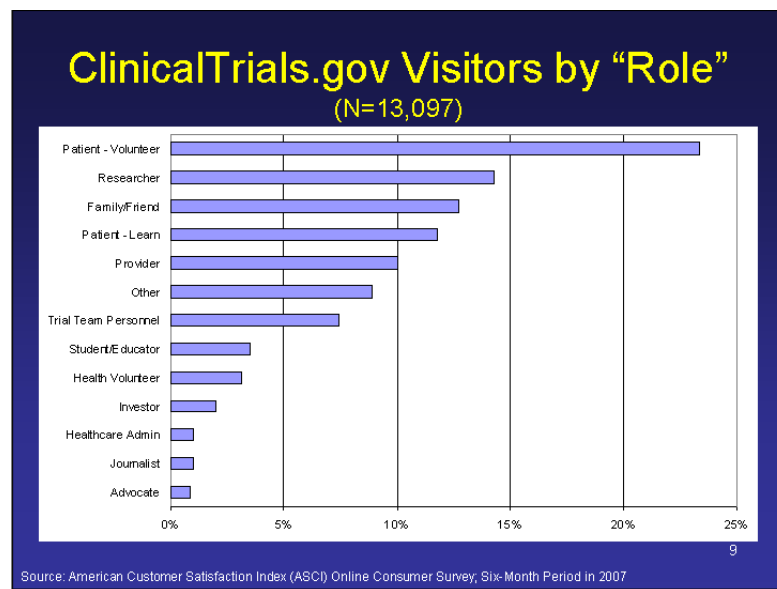


Figure 1: "Patient – Volunteer" is the most common user of this database; "Family/Friend" is third.

Today, ClinicalTrials.gov provides essential functions for patients and researchers, but the task of finding clinical setting-appropriate studies remains daunting, due in part to the

success of ClinicalTrials.gov: the overwhelming number of studies one must review, as illustrated by a simple search for Lymphoma and CLL studies:

The screenshot shows the ClinicalTrials.gov website interface. At the top, there is a search bar with the text "Found 1086 studies with search of: lymphoma [CONDITION] OR CLL [CONDITION] | Open Studies". Below the search bar, there are several navigation buttons: "List Results", "Refine Search", "Results by Topic", "Results on Map", and "Search Details". The main content area displays two recruiting studies. The first study is titled "Ph I/II Study of Subcutaneously Administered Veltuzumab (hA20) in NHL and CLL" and lists various conditions such as NHL, Lymphoma, Non-Hodgkin, Lymphoma, B-Cell, Lymphoma, Follicular, Lymphoma, Intermediate-Grade, Lymphoma, Large-Cell, Lymphoma, Low-Grade, Lymphoma, Mixed-Cell, Lymphoma, Small-Cell, Leukemia, Lymphocytic, Chronic, Leukemia, B-Cell, Chronic, Leukemia, Prolymphocytic, Leukemia, Small Lymphocytic, Lymphoma, Small Lymphocytic, Lymphoma, Lymphoplasmacytoid, CLL, Lymphoplasmacytoid Lymphoma, CLL, CLL, SLL. The second study is titled "Study of MLN8237 in Patients With Advanced Hematological Malignancies" and lists conditions such as B-Cell Follicular Lymphoma, B-Cell Marginal Zone Lymphoma, Diffuse Large B-Cell Lymphoma, B-Cell Mantle Cell Lymphoma, B-Cell Small Lymphocytic Lymphoma (SLL), B-Cell Chronic Lymphocytic Leukemia (B-CLL), Multiple Myeloma, and Waldenstrom's Macroglobulinemia.

Figure 2: November 21, 2008: Search for lymphoma and CLL clinical trials: 1086 studies found.

For patients, the challenge of using the registry is how to locate the studies, among many hundreds, that may be appropriate to our needs and circumstances:

- Our treatment history
- Our treatment goals
- Patient and disease characteristics

We ask:

- Is it feasible to enable searchers of ClinicalTrials.gov to locate studies that may address human needs and clinical circumstances?
- Might expanded search functions mitigate the very low enrollment rates in clinical trials for cancers?
- Might adding eligibility search fields also help to shape the design of clinical trials in positive ways?

We start by providing patient circumstances, which require translation into database structure:

- I have lymphoma but have *never had treatment*. I want to consider studies that have curative potential, because standard therapies are not yet curative.
- I'm *elderly* and in *poor health*. I require a therapy that has *lower expected toxicities* than standard treatments.
- I have indolent lymphoma and do not require therapy, but I'd like to consider study protocols of a type that are *low risk*, that may slow progression and are also unlikely to preclude benefiting from standard therapies later on.
- I have disease that is *refractory* to standard protocols. I have an urgent need to locate study protocols of new agents with *unique mechanisms of action*.

- I need to consider studies that are aggressive, which include allogeneic stem cell transplantation, due to having *high-risk disease* and *recent bone marrow failure*.

Here we propose what we believe to be a feasible and needed enhancement, as a draft. The addition of search fields that relate to clinical circumstances and treatment objectives to complement existing **Targeted Search** fields shown in Figure 3.

Ideally, the new fields can provide also conditional choices in a drop-down list. That is, if the chosen **Condition** is *lymphoma*, the **Grade** list box will show options specific for that type of cancer, such as *indolent* and *aggressive*.

We recognize that a change to a registry of this magnitude would also require the sponsors to update each protocol, and have proposed how this might be done below.

Figure 3: Targeted Search fields as of November 2008

USER CONSIDERATIONS

Ultimately, the value of a registry is that it can provide answers for its primary users. The ASCI survey (Figure 1) shows that users of the Clinicaltrials.gov registry have diverse skills and backgrounds. Patients and patient surrogates, representing the largest segment of primary users, will require an interface that continues to use plain language and uncomplicated formats – a tiered approach, as done now with the Basic and Advanced Search forms.

PROPOSING FOR CONDITION:

Condition: *Unspecified, Cancer type (as in SEER)*

Grade *Unspecified, Aggressive, Indolent, Either*

Cell type: *Unspecified, T-cell, B-cell, NK cell, Other*

Histology (cell type) *Unspecified, DLBCL, Follicular, CNS, MCL, CLL/SLL, Other*

Stage *Unspecified, Localized (stage I / II), Widespread (III – IV)*

NOTE: We recognize that some of the fields in this group may be challenging to implement given the number of disease subtypes for cancers and other life-threatening conditions.

PROPOSAL FOR CLINICAL SETTING SEARCH FIELDS:

** Searchable categories with an asterisk are considered very important to locating studies that may be appropriate to a patient's clinical setting. The notes we provide are proposed descriptions to help users identify the meaning of a field name.*

Treatment History *

Previously treated? *Unspecified, Yes, No, Either*

Time since last therapy *Unspecified, Months*

Refractory *Unspecified, Primary, Secondary, Either*

Group Note: Treatment History is thought to be a primary determinant for eligibility. The ability to exclude studies that are for Refractory, or Previously treated patients has been cited by patients as most important.

Patient and Disease Characteristics

Age *Unspecified, Child, Adult, Age in Years*

Performance index *Unspecified, High, Intermediate, Low*

Disease risk *Unspecified, High, Intermediate, Low, Variable*

Common disease exclusion criteria *(such as CNS or HIV)*

Common patient status exclusion criteria
(such as Bone marrow, Liver and Kidney function)

Group Note: Many times patients will locate studies of interest only to learn they are not eligible because of age, or performance, or other reasons. It's our hope that study protocols can be quickly found or excluded by specifying patient and disease characteristics at the start of the search.

Treatment Goals *

Durable remission/curative *Unspecified, Yes, No*

~ Treatment indicated or required

~ Higher anticipated toxicity, offset by potential for disease free outcome

~ Generally for aggressive disease, or higher-risk indolent disease

Alternative to observation *Unspecified, Yes, No*

~ Treatment and prior therapy not indicated or required

~ Lowest anticipated toxicity – transient and reversible

~ Low anticipated risk to preclude benefit from standard therapies

~ Generally for lower-risk, indolent disease

Management *Unspecified, Yes, No, Either*

- ~ Similar to Alternative to Observation, but with need to treat.
- ~ Toxicity profile: agents with transient or low toxicity
- ~ Low anticipated risk to preclude benefit from standard therapies
- ~ Generally for low-risk, indolent disease; or relapsed aggressive disease

Symptom relief (palliative) *Unspecified, Yes, No, Either*

Group Note: These might be considered mutually exclusive goals with limited potential for overlap. We appreciate that risk is not always possible to anticipate and is dependent on many factors, known and unknown. A disclaimer might be required to highlight the uncertainty about risk as it relates to the goal of therapy. We think this is worth the effort because the goal of therapy is often the starting point from which patients and physician focus on what type of therapy is most appropriate, clinically.

Treatment Type:

Administration: *Unspecified, Single agent, Sequential, Combination, Consolidation*

Dose Finding *Unspecified, Yes (fixed / graduated), No*

Prognostic biomarkers *Unspecified, Yes, No*

We think of Prognostic biomarkers as tests of biological samples (blood, tumor) that may predict response or toxicity to study agents. Informed patients consider identifying biomarkers of response and toxicity as vital to making clinical progress, in order to lower the risk of unproductive toxicity from ineffective treatments in future – a risk of primary concern to patients, because of its impact on quality of life and the ability to benefit from subsequent therapy.

Treatment Class:

Immunotherapy *Unspecified, Adoptive, Antibody, Vaccinal / Immune modulating (Or Yes/No)*

Chemotherapy-based *Unspecified, Yes, No*

Chemo-immunotherapy *Unspecified, Yes, No*

Radioimmunotherapy-based *Unspecified, Yes, No*

Stem Cell rescue? *Unspecified, Yes, No*

Type: *Unspecified, Allo / Auto / Nonmyeloablative, Cord Blood, Other*

Targeted *Unspecified, Yes, No*

- ~ Study agent has high specificity for the tumor cell or microenvironment

Group Note: Ideally new classes of therapy could be appended by sponsors as needed, with a centralized verification procedure to ensure there's no overlap or inconsistencies in terminology.

HOW SPONSORS MIGHT UPDATE THE REGISTRY PROTOCOLS

We anticipate the new search fields could be entered efficiently by sponsors, utilizing a centralized web-based **Protocol Update form**; and that this form would be similar to the user's **Advanced Targeted Search form**, if not identical.

As you know, use of drop-down lists, option buttons, and check boxes will simplify the process, and also facilitate uniform field entries. Templates might be provided for common clinical settings, mitigating the need to modify each field; and sponsors might save protocol answer sets to be reused when updating similar protocols in future.

HOW PATIENTS MIGHT SEARCH THE ENHANCED REGISTRY

From **Basic** or **Advanced Targeted Search forms**, patients, caregivers, volunteers, organizations, or physicians need only select from drop-down lists to enter patient-specific criteria for the purpose of efficiently locating candidate studies.

Pop-ups might be used to describe the meaning of the technical fields for laypersons, such as *Prognostic biomarkers* with an explanation also to select *Unspecified* if the meaning is not known or is not important to the search.

The search criteria can be saved with user-provided names so that the registry question (the query) can be reused in future by the same patient or by others with similar needs.

IN SUMMARY

Benefits to Registry Users

As you know, standard treatments are not always effective against many cancers, which continue to cause considerable pain, suffering and death. Thus, patients look also to clinical trials ... for promising new agents, and new uses of existing treatment agents, offering at least the potential for better outcomes.

Obviously, patients and treating physicians cannot consider what they don't know to exist, and the challenge of locating appropriate studies has been cited by at least some oncologists as a reason for not referring patients to clinical trials.¹ We note that locating clinical studies is almost certainly the primary need of the primary users of the registry!

Enrollment in clinical trials is widely acknowledged to be insufficient to support progress against cancers (3-5%). As drug discovery accelerates, the evaluation bottleneck will get worse: Thousands of new agents, instead of hundreds, but the same number of patients and the same obstacles to enrollment (the ability to locate studies among them), which are undoubtedly delaying innovations.

Other Benefits:

We anticipate that the proposed search enhancements would likely improve also clinical trial enrollment if implemented, potentially lowering research costs and accelerating progress against life-threatening disease.

Also, a more structured database will allow the NIH and investigators to easily identify important patterns in clinical research and study design.

Finally, requiring clinical setting-based search fields might also help investigators to design studies with greater sensitivity to addressing a key obstacle to clinical trial enrollment: that

¹ Clinical Trial Survey for Physicians Treating Lymphomas, Preliminary results
<http://www.lymphomation.org/ds-report.pdf>

each study protocol be also a reasonable treatment decision – that it compares well with other studies in this regard for a given treatment setting.²

We therefore urge the National Institute of Health to implement at least *some aspects* of our proposal to enhance the search capabilities of the ClinicalTrials.gov registry ... to further enhance a vital public resource.

Thank you for taking time to consider our proposal. We look forward to your response.

Sincerely,

A handwritten signature in black ink, appearing to read 'Karl Schwartz', with a long horizontal flourish extending to the right.

Karl Schwartz

President and co-founder, Patients Against Lymphoma

Patient Consultant to the FDA/Oncologic Drug Advisory Committee (ODAC)

Participant: NCI Progress Review Group for Blood Cancers (LMPRG)

Participant: Biospecimen Access and Ethical, Legal, and Policy Issues Workshop (ELP)

Participant: Custodianship and Ownership Issues in Biospecimen Research Symposium

² Schwartz, K, 2008, Lymphoma and Myeloma International Conference, Interests, attitudes, and participation in clinical trials among patients with lymphomas (with online access) <http://www.lymphomation.org/IAP.pdf>

APPENDIX

Here is a screenshot of our clinical trials resource, which illustrates that we have direct experience in assisting patients with study searches. On this page and sub-pages we provide ready-made queries of the ClinicalTrials.gov registry to help patients find studies specific to their condition.

[Treatments](#) > Clinical Trials

Last update: 10/24/2008

Search for Clinical Trials by Location:



by [State](#) or [World ... CLL](#) or [Lymphoma](#) specific

by treatment type	by lymphoma subtype	Other New	by State or Country
Includes links to related PubMed abstracts	Includes filters for newly diagnosed or recurrent disease All studies for Lymphomas	Includes filters for age, alternative Med, fatigue, first-line, grade, phase, stage, and refractory disease Phase III trials for lymphoma indolent aggressive	Locate lymphoma studies in your state or country

NCI-sponsored trials for Lymphoma [Cancer.gov](#)

[New search tool](#) [WHO International Clinical Trial Search](#)

New clinical trials since:
[Sep](#) | [Aug](#) | [July](#) | [Jun](#) | [May](#) | [Apr](#) | [Feb](#) | [Jan](#) | [Last Year](#)

Clinical trials of interest for Lymphoma:
[First Line Low Toxic](#) | [First Line Primary Therapy](#) |
[Relapsed / Refractory Lymphoma](#) | [Other unmet needs](#)

Figure 4: Patients Against Lymphoma resource – providing ready-to-use queries of ClinicalTrials.gov