

Patients Against Lymphoma



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STUDY PROPOSAL

Combine molecular profiling research with evaluating first-line use of patient-specific idiotype cancer vaccines

KEY BENEFITS: Acquire tissue once for multiple and complementary purposes. Avoid ethical issue of acquiring tissue solely for basic research. Quickly accrue patients for important clinical and basic research without precluding optimal benefit from standard treatment in future.

BACKGROUND: Patient interest is an important starting point for study design. Patients with untreated stable disease provide an important untapped opportunity to investigate immune therapies, while also increasing our understanding of the molecular biology of the disease – which can provide the context for understanding outcomes, and the variable clinical course of this incurable and common disease.

PROPOSAL: Combine molecular profiling research (*what is needed to inform all research*) with evaluating first-line use of patient-specific idiotype therapeutic cancer vaccines (*what patients want*).

CONDITION: Previously untreated indolent follicular lymphomas who are in watchful waiting status - have stable disease and modest or low tumor burden.

BENEFITS:

- Acquire tissue once for multiple and complementary purposes.
- Foster multidisciplinary and coordinated research.
- Avoid ethical issue of acquiring tissue solely for basic research, or solely to test an investigational treatment.
- Provide an opportunity to involve patients with indolent lymphomas in important research, without precluding optimal benefit from standard treatment in future; when the participants have stable disease and better immune competence - no prior exposure to immune suppressing therapies.
- Achieve very fast enrollment because of the favorable expectations among patients about cancer vaccines - a chance to avoid or delay cytotoxic therapies that are not curative.

Patient interest in first-line idiotype vaccines appears to be very high based on a recent informal survey. This finding is further supported by the time it took to fully enroll patients in a cancer vaccine pilot study conducted at Stanford University Medical Center in 2000: just two weeks.

- Provide a proactive alternative to patients with an incurable and most common type of indolent lymphoma.
- Watchful waiting status is often described as watchful worrying. For these patients quality of life can be impaired significantly by stress related to ongoing concerns about unseen progression and accumulations of mutation. Each physician sensation, whether connected to progression or not, increasing the level of stress.*
- While under study the participants will benefit from having more routine monitoring and closer supervision.
 - We may anticipate that what is learned in this special population will carry over to other treatment settings, and subtypes of lymphoma.
 - Importantly, this research can provide insights into immunity that will cross over to numerous health conditions, such as autoimmune disease.
 - We anticipate that one or more of the current sponsors of idiotype vaccines will have an interest in co-sponsoring the study. Genitope and Favrilite have completed enrollment in phase III studies; and Biovest, who has not completed enrollment in it's phase III study, although it began first.
 - Finally, combining these research initiatives will help to rapidly answer important study questions listed below.

CLINICAL STUDY QUESTIONS

First line idiotype vaccine in untreated follicular lymphoma with stable disease

- Can idiotype cancer vaccines induce active immunity against tumors?
- Can inducing active immunity delay the need for cytotoxic therapies without quality of life penalties, and toxic side effects associated with cytotoxic therapy?
- Can inducing active immunity lead to reduction of tumor burden?

Secondary:

- Identify biomarkers of immune response, or that predict same.
- Discover the effect of dose and scheduling on Immunogenicity.
- Identify biomarkers that correspond to immune response and/or clinical benefit.
- Identify biomarkers that correspond to disease progression.
- Identify the predictive role of polymorphisms specific to active immunotherapy.
- Identify how tumors may escape or suppress immunity.
- Identify the potential role of T-regulatory cells in anti-tumor immunity.

BASIC RESEARCH STUDY QUESTIONS:

Molecular profiling of tumor and microenvironment of untreated indolent follicular lymphomas

- Characterize the molecular biology of indolent follicular lymphomas
- Identify molecular markers of tumor suppression of immunity or Immunogenicity.
- Identify host/tumor interactions, and distinct profiles of these interactions.
- identify molecular targets for therapy.
- Identify molecular basis of prognostic subtypes
- Identify molecular basis for clinical aggressiveness or indolence.
- Identify biomarkers that may correlate with responses to subsequent treatments.

ONE APPROACH TO DE-IDENTIFYING CLINICAL DATA:

Each study group would publish findings to the Bioinformatics system (BIS) using de-identified coded data as described in the NBN blueprint.

Code creation: The primary code is entrusted to an honest broker, and a second unique code, a clinical code, is generated - one code mapped to the other, using a randomized software routine.

Tissue and code: The molecular profiling group receives the de-identified, annotated tissue with the primary code. The vaccine study group receives the tissue with the clinical code.

Publishing: (1) The clinical data is de-identified and replaced with the clinical code, and published to the BIS through the honest broker. (2) The honest broker replaces the clinical code with the primary code using an automated system. (3) The honest broker then forwards the clinical data to the BIS.

In this way, the clinical investigators do not know the personal identity of the data as it appears in the BIS even though they provide it.