

IES, Inc. Satellite Clinical Workshop

Title: Therapy for Rare Eosinophilic Disorders: Clinical Trial Design and Endpoint Validation

Rare disease(s) represented: hypereosinophilic syndrome, eosinophilic gastrointestinal disorders (EGID), Churg-Straus vasculitis, eosinophilic pneumonia, episodic angioedema and eosinophilia (Gleich's syndrome)

Meeting date: June 21, 2010

Meeting location: Quebec, Canada

Sponsoring Organization: International Eosinophil Society, Inc.

Organizational Contact: Joan Geiger
Executive Director, International Eosinophil Society, Inc.
555. East Wells Street, Suite 1100
Milwaukee, WI 53201
Tel: 414-276-6445
Fax: 414-276-3349
Email: jgeiger@eosinophil-society.org

Program Contact: Amy Klion, MD
President-Elect, International Eosinophil Society, Inc.
224 Wendover Rd
Baltimore, MD 21218
Tel: 410-963-4420;
Fax: 410-889-4076;
Email: amy@zunkeler.com

Javed Sheikh, MD
Clinical Director, Division of Allergy and Inflammation
Clinical Director, Center for Eosinophilic Disorders
Beth Israel Deaconess Medical Center/Harvard Medical School
One Brookline Place, Suite 623
Brookline, MA 02445
Division Office: 617-278-8100
Fax: 617-278-8101
Email: jsheikh@bidmc.harvard.edu

Rationale:

Rare eosinophilic disorders, including hypereosinophilic syndrome (HES), Churg-Strauss vasculitis, and eosinophil-associated gastrointestinal disorders (EGID), are a heterogeneous group of disorders that are characterized by marked eosinophilia in the peripheral blood and/or tissues without a secondary cause. Although recent data from a multicenter, retrospective study of 188 patients with HES suggest that steroids are effective initially in most patients with HES, a majority of patients become steroid-refractory or develop significant steroid toxicity. Conventional second line agents, including hydroxyurea and interferon-alpha, are only effective in approximately 30% of patients and have undesirable side effect profiles. Thus, better agents are clearly needed to treat patients with these disorders.

Recent advances in drug design have led to the creation of a wide variety of agents that target specific molecules involved in disease pathogenesis. One of these, imatinib, a tyrosine kinase inhibitor developed for the treatment of CML, has revolutionized the treatment of patients with a myeloproliferative variant of HES/chronic eosinophilic leukemia, and became the first drug FDA-approved for the treatment of HES. A second agent, mepolizumab (a monoclonal antibody against interleukin 5 initially developed for the treatment of asthma) has been shown in a multicenter, placebo-controlled international trial to have

remarkable efficacy with little or no toxicity in the treatment of steroid-responsive HES (Rothenberg et al. 2008 N Engl J Med). Unfortunately, with the exception of imatinib, no agents have been FDA-approved for the treatment of these disorders. This is likely due to a combination of factors, including limitations on patient accrual (22 centers worldwide were necessary to accrue the 84 subjects needed for the mepolizumab trial) and the lack of validated clinical trial endpoints for these complex disorders.

Having a meeting focused on clinical studies of eosinophilic disorders is timely since the first registry for eosinophilic disorders (REGID) (www.regid.org) has been recently launched. REGID provides an opportunity for the meeting participants to become REGID members and design studies that will be facilitated by REGID.

Format:

As with the four prior clinical workshops held in association with the biannual meeting of the International Eosinophil Society, we anticipate a total of approximately 30-40 participants with clinical and/or research expertise in eosinophilic disease and/or clinical trial design. The workshop will be divided into two parts. The first part will consist of brief state-of-the-art reviews of HES, CSS and EGID highlighting issues pertinent to clinical trial design (diagnostic criteria, definition of response to therapy, biomarkers of disease activity). This will be followed by presentations from experts in clinical trial design for complex rare diseases from academia, industry and the FDA (not confirmed). The second part of the symposium will be comprised of small group discussions designed to troubleshoot specific issues facing ongoing or planned clinical trials in HES, CSS and EGID.

Goals:

The short-term goals of the workshop are: 1) to bring individuals from academia, the FDA, and industry with expertise in clinical trial design for complex disorders together with clinician-scientists with expertise in rare eosinophilic disorders to discuss validation of clinical trial endpoints and clinical trial design and 2) to continue to foster collaborative relationships between multidisciplinary clinical and basic science researchers interested in eosinophilic disorders. It is anticipated that the findings from this workshop will lead to a prospective, multicenter trial designed to validate endpoint criteria for disease flares in one or more rare eosinophilic disorders. Ultimately, this will lead to improved design of planned multicenter clinical trials to assess the safety and efficacy of novel agents for the treatment of these disorders.

Draft Agenda:

8:30-9:00	Opening Remarks/Introductions – Amy Klion (confirmed)
9:00-10:30	Outlining the problems
9:00-9:30	HES Peter Weller (confirmed)
9:30-10:00	CSS Michael Wechsler (confirmed)
10:00-10:30	EGID Marc Rothenberg (confirmed)
10:30-11:00	Coffee Break
11:00-11:30	Successful clinical trial design for complex disorders - Peter Merkel (confirmed)
11:30-12:00	Rare diseases, clinical trial design and the FDA – to be determined
12:00-12:30	Drug development for rare diseases: a company perspective - Jeff Wilkins, Cephalon (confirmed)
12:30-1:30	Lunch
1:30-2:00	Statistical approaches to endpoint validation -Vern Chinchilli (confirmed)
2:00-2:30	Disease registries as a tool for multicenter trials of rare disorders - James Franciosi (confirmed)
2:30-4:30	Small group discussions

If you are interested in attending and have not yet received information by email, please contact Amy Klion at aklion@eosinophil-society.org