Progress Report: Date: 9/20/14

Project: ASFA Registry Study

To date there has been steady progress since the registry was IRB approved last year. There are currently 40 patients that have been retrospectively added to the database. These include 15 Neuromyelitis Optica patients, 10 Wilson's disease patients, and 15 MUSK positive Myasthenia Gravis patients. Two oral abstracts have been submitted, one on the current status of the registry and another on a preliminary analysis of the Wilson's disease patients. Currently data on the Wilson's disease is being analyzed for manuscript preparation.

Wu Y, Cooling L, Fernando LP, Hofmann J, Kim HC, Morgan S, Pagano M, Perumbeti A, Pham HP, Schneiderman J, Sachais B, Schwartz J, Shi P, Winters J, Yamada C, **Wong ECC** (2014) Report of the ASFA apheresis registry. Presented at the ASFA National Meeting, San Francisco, CA, April 2014 (oral presentation).

Wu Y, Pham HP, Morgan S, Yamada C, Cooling L, Kim HC, Schneiderman J, Sachais B, Schwartz J, Winters JL, Hofmann J, Pagano M, **Wong ECC**. Report of the ASFA registry study on Wilson's disease. Presented at the ASFA National Meeting, San Francisco, CA, April 2014 (oral presentation).

Amendments since the last continuing review:

The study was amended on 5/7/14 to add the PI's name, address and contact information at the top of the research protocol, added version 030814 to the title of the protocol, updated the membership of the ASFA committee, clarified the number of total participants that will be enrolled from a multicenter perspective, added the diseases that are currently being studied and updated the references.

These requested changes are largely for clarification and adminstrative purposes.

Respectfully submitted,

Edward Wong, MD

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SINGLE-CENTER EVALUATION OF CHANGES IN INDICATIONS OF APHERESIS PROCEDURES PERFORMED IN RESPONSE TO PUBLICATION OF UPDATED GUIDELINES FOR THE USE OF THERAPEUTIC APHERESIS

Briana Gibson, MD, Steven A. Mann, MS III, Lawrence Williams, MD, and Marisa B. Marques, MD
University of Alabama at Birmingham, Birmingham, Alabama

Purpose: In June of 2007, The Journal of Clinical Apheresis published its first evidence-based guidelines for therapeutic apheresis. Updates to these guidelines have been published in June of 2010 and most recently, June 2013. These guidelines classify disease states into categories based on the strength of evidence available in the literature. In this report, we decided to determine what percentage of therapeutic plasma exchanges (TPE) and extracorporeal photopheresis (ECP) procedures performed at our institution fell into the three main indication categories established by the guidelines (I, II, and III). Additionally, we sought to determine if the publication of each set of guidelines in 2007 and 2010 translated into changes in the conditions we treated.

Methods: We collected data on all apheresis procedures performed at our institution from July 01, 2007 to June 30, 2010 and from July 01, 2010 to June 30, 2013, to coincide with the timing of the publication of the ASFA guidelines in 2007, 2010, and 2013. We compiled this list from our database of apheresis records and cross-referenced each procedure with the category in the guidelines that were current at the time of the treatment. As needed, patient information was supplemented with review of the electronic medical record. We used Microsoft Access as the database platform, and Microsoft Excel for data analysis.

Results: From July 2007 to June 2010, 1,842 TPE and 1,361 ECP procedures were performed in our institution. By category, TPE procedures were 49% Category I, 15% Category II, and 28% Category III. ECP procedures were 48, 16, and 33% of each category, respectively. From July 2010 to June 2013, the total number of patients treated with TPE increased to 2,182 with 74% of those being Category I procedures. Category II indications decreased to 7% and Category III to 10%. Total ECP procedures for the same time-period increased to 1,679, with Category I procedures falling slightly to 40%, while Category II procedures increased to 56% of the total, while Category III indications fell to 4%. The top five diagnoses in the 2007–2010 dataset were solid organ transplant rejection (SOTR, 40% of total procedures), graft-versus-host disease (GVHD, 9%), myasthenia gravis (MG, 8%), cutaneous T-cell lymphoma

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REPORT OF THE ASFA APHERESIS REGISTRY

Yanyun Wu, MD, PhD,[1,2] Laura Cooling, MD,[3] Leonor P. Fernando, MD,[4] Jan Hofmann, MD,[5] Haewon C. Kim, MD,[6] Shanna Morgan, MD,[7] Monica Pagano, MD,[2] Ajay Perumbeti, MD,[8] Huy P. Pham, MD, MPH,[9,10] Jennifer Schneiderman, MD, PhD,[11] Bruce Sachais, MD, PhD,[12] Jospeh Schwartz, MD,[9] Patricia Shi, MD,[10] Jeffrey Winters, MD,[13] Chisa Yamada, MD,[3] and Edward C.C. Wong, MD[14]

[1]Yale University, New Haven, Connecticut
[2]Puget Sound Blood Center, Seattle, Washington
[3]University of Michigan, Ann Arbor, Michigan
[4]University of California, Davis, Davis, California
[5]California Pacific Medical Center, San Francisco, California
[6]Children's Hospital of Philadelphia, Philadelphia, Pennsylvania
[7]University of Minnesota, Minneapolis, Minnesota
[8]Children's Hospital of Los Angeles, Los Angeles, California
[9]Columbia University, New York, New York
[10]New York Blood Center, New York, N York
[11]Children's Memorial Hospital, Chicago, Illinois
[12]University of Pennsylvania, Philadelphia, Pennsylvania
[13]Mayo Clinic, Rochester, Minnesota
[14]Children's National Health System, Washington, District Columbia

Purpose: Therapeutic apheresis procedures have been applied to the treatment of many rare diseases and rare indications for more common diseases. Because of a limited number of patients and cases, it has been very difficult to collect evidence for the efficacy of apheresis in these disorders or indications. Only a limited number of anecdotal reports or small cases series have been reported in the literature, requiring single institutions to perform difficult and extensive retrospective studies in order to assess the clinical efficacy of therapeutic apheresis for a rare disorder or indication. The lack of a consistent and comprehensive reporting mechanism often produces an incomplete or biased clinical description of the apheresis experiences. To establish a mechanism to report and collect apheresis data in a standardized format, an ASFA REDCap disease registry was developed by the ASFA apheresis registry subcommittee.

Methods: ASFA apheresis registry subcommittee of the Applications committee determined the specific diseases and conditions that were initially included in this study. This was followed by construction of the REDCap database that was hosted at Children's National Health System including the incorporation of clinical assessment instruments. The following conditions were included for the registry study: Wilson's disease

(WD), neuromyelitis optica (NMO), and muscle specific kinase (antibody positive) myasthenia gravis (MUSK+ MG). The registry includes patient demographic and clinical information, apheresis procedural information, treatment schedule, and treatment outcome/complications. Both prospective and retrospective data with the latter involving data collection back to January 2000 are allowed in the registry.

Results: To date, a total of 15 centers have indicated interest in participating in the registry with eight institutions preparing their IRB submission, three awaiting IRB approval, and five IRB approved institutions, actively entering data. Of the 15 centers, three (20%) include pediatric academic hospitals, 11 (84%) predominantly adult academic centers, and one (7%) community hospital (with an active research focus). Based on Census Bureau defined regions: four (27%), four (27%), five (33%), and two (13%) centers are located in the West, Midwest, Northeast and South regions, respectively. Estimated potential accrual for NMO, WD, and MUSK+ MG are 38, 19, and 14, respectively. Based on the average number of plasma exchange procedures at each institution per year in fiscal year 2013, the scope of the registry covers at least 6,050 procedures per year ($n = 10$ centers reporting, range 75 to 1,100 procedures/yr). At the current time, 10 WD patients have been entered from five institutions, with enrollment of patients just beginning for NMO and MUSK+ MG.

Conclusion: Establishing a registry for apheresis will enable ASFA to gather apheresis experiences from multiple centers effectively. Such information will enable us to evaluate the efficacy of apheresis for rare apheresis indications. ASFA, as a national organization for Apheresis Medicine, is in a perfect position to lead and to carry out this multiinstitutional project.

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REPORT OF THE ASFA APHERESIS REGISTRY STUDY ON WILSON'S DISEASE

Yanyun Wu, MD, PhD,[1] Huy P. Pham, MD, MPH,[2] Shanna Morgan, MD,[3] Chisa Yamada, MD,[4] Laura Cooling, MD,[4] Haewon C. Kim, MD,[5] Jennifer Schneiderman, MD,[6] Bruce Sachais, MD, PhD,[7] Joseph Schwartz, MD,[8] Jeffrey L. Winters, MD,[9] Jan Hofmann, MD,[10] Monica Pagano, MD,[11] and Edward C.C. Wong, MD[12]

[1]Yale University, New Haven, Connecticut
[2]Columbia University and New York Blood Center, New York, New York
[3]University of Minnesota, Minneapolis, Minnesota
[4]University of Michigan, Ann Arbor, Michigan
[5]Children's Hospital of Philadelphia, Philadelphia, Pennsylvania
[6]Children's Memorial Hospital, Chicago, Illinois
[7]University of Pennsylvania, Philadelphia, Pennsylvania
[8]Columbia University, New York, New York
[9]Mayo Clinic, Rochester, Minnesota
[10]California Pacific Medical Center, San Francisco, California
[11]Puget Sound Blood Center, Seattle, Washington
[12]Children's National Health System, Washington, District Columbia

Purpose: Wilson's disease is a rare autosomal recessive genetic disorder (1:30,000) of the ATP7B gene that results in copper accumulation in the liver, brain, cornea and kidney. Even though there are available treatment options such as low-copper diets, zinc acetate, tetrathiomolybdate and copper chelation, patients may still present in crisis either before their disease is diagnosed, or after diagnosis due to ineffectiveness or intolerance to current therapy. Patients with Wilson's disease crisis often present with fulminant hepatic failure, severe DAT-negative hemolytic anemia and multiorgan failure, with rapid clinical deterioration. Eventually many patients require liver transplantation. In this setting, therapeutic plasma exchange (TPE) has been used to remove copper and provide a bridge to liver transplantation. Most studies describing the use plasma exchange for Wilson's disease have been case reports. Here we report the collective experiences through the ASFA apheresis registry on Wilson's disease.

Methods: The ASFA apheresis registry study is a multicenter registry study. Both prospective and retrospective data with the latter involving data collection back to January 2000 are allowed in the registry. Study data were collected and managed using REDCap electronic data capture tools hosted at Children's National Health System. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies. The registry includes patient demographic and clinical information, apheresis procedural information, treatment schedule, and treatment outcome/complications. All participating sites had obtained approval from the ASFA apheresis registry subcommittee of the ASFA Applications committee as well as from local IRBs.

Results: To date, a total of 10 patients (three males and seven females) with Wilson's disease treated between 2005 and 2013 were included in this study. Median age of first diagnosis was 16-years-old (range 6–30 years). Median age at first TPE was 17 years (range 6–61 years). The patients underwent a total of 43 TPEs with most of patients requiring an intensive session of TPE. Median number of TPE procedures was 3.5 (range 1–9). Other than one patient who had received one TPE before the patient was transferred to the study site, no patient received TPE prior to the first registry study TPE. All of the TPEs used ACD-A as anticoagulation, 98% (42/43) TPEs targeted 1–1.25 plasma volumes, and 95% (41/43) TPEs were performed with 100% fluid balance. All patients had a central line placed for TPE. Post TPE, 90% (9/10) patients underwent liver transplantation, all 10 patients (transplanted as well no transplanted) have at least a 6-month survival.

Conclusion: All 10 patients with Wilson's disease who underwent plasma exchange had a positive outcome in terms of 6-month survival. As a first report of the ASFA apheresis registry study, we demonstrated the value of using this registry to collect apheresis related patient outcome from multiple centers.

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GREATER THAN NINETY PERCENT OF PATIENTS WITH ACUTE LEUKEMIA AND HYPERLEUKOCYTOSIS WHO RECEIVE LEUKOCYTAPHERESIS TREATMENT SUCCESSFULLY UNDERGO INDUCTION CHEMOTHERAPY: FOLLOW-UP ANALYSIS OF DATA FROM 2006–2013.

Jan C. Hofmann, MD, MPH,[1,2] Kathleen M. Grant, MD,[1] and Dobri D. Kiprov, MD[1,2]

[1]California Pacific Medical Center, San Francisco, California
[2]Apheresis Care Group, San Francisco, California

Introduction: A number of retrospective, cohort studies have demonstrated that leukocytapheresis (Lp) treatment in patients