THE ASFA DISEASE REGISTRY: A PROGRESS REPORT

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Disclosures

- Non-relevant
- Employee of Quest Diagnostics
April/May 2010  As a result of leadership by Drs. Zbigniew “Ziggy” Szczepiorkowski and Yan Yun Wu, this registry endeavor started out within the ASFA Clinical Applications Committee, initially chaired by Yan Yun Wu, and co-chaired by Edward Wong.

October 2012  IRB approval for the research protocol by Children’s National followed by REDCap databases for Wilson’s Disease, Neuromyelitis Optica and MUSK+ Myasthenia Gravis, moving into production July 29, 2013.
## History

### Special Research Ad-hoc Committee: Beginning and Evolution

<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
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<tbody>
<tr>
<td>Winter 2011</td>
<td>Chris Chun, ASFA’s current president, creates a new ad-hoc committee, named the ASFA Research Special Committee, to foster research and networking among the ASFA membership. Ed Wong chairs committee.</td>
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<td>April 2012</td>
<td>Became Research Subcommittee, under Applications Committee because of its research focus. Charges developed.</td>
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<td>Spring 2015</td>
<td>Merges with Rare Disease Registry Committee to satisfy research priorities of ASFA and because of the similarity in focus to become new Research Subcommittee of the Applications Committee.</td>
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<td>May 2015</td>
<td>Presentation to the Board to create a new standing Research Committee. Approved by the Board.</td>
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<tr>
<td>May 2016</td>
<td>Bylaws changed at annual meeting to create a new Research Committee.</td>
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The Research Committee: The Beginning (2016)
Why a Multi-Institutional General Registry Approach?

- Allow for systematic collection of detailed clinical and procedural information for the efficacy assessment and determination of side effects in a consistent fashion.

- Allow for the rapid collection of clinical, laboratory and procedural data for multiple diseases/indications.

- Weaknesses of all previous apheresis registries included:
  a) Lack of detailed apheresis procedure data
  b) Lack of detailed clinical and laboratory data
  c) Lack of outcome data
  d) Single site
1. To enhance ASFA’s research mission by educating ASFA members of potential sources of current and future extramural research funding for donor and therapeutic apheresis.
2. To work or promote interaction with relevant government and private agencies in seeking funding opportunities (including new funding mechanisms or pathways) for Apheresis Medicine
3. To promote discussion and collaboration in the identification and prioritization of key research questions related to Apheresis Medicine (such as organizing ASFA workshop or forum on research)
CHARGES

4. To facilitate networking of apheresis centers and/or practitioners for the advancement of research in Apheresis Medicine.
What Are Key Elements in a Multi-institutional Registry Study?

- Centralized Research Plan
  - DUAs/IRB Applications
- Operations Manual
  - To define policies/procedures
- Data Entry
  - Central database (REDCap)
- Statistical Analysis/Support
- Writing Groups/Publication

Time significantly shortened if already in Place!

- 1-2 years
- 6 mo – 1 yr
Current ASFA Registry Sites (as of 3/24/17)

- Active, enrolling (n=12)
- IRB approval pending (n=1)
- Interested, IRB yet not submitted (n=6)
ASFA Registry Results

Registry Participants as of March 2017

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<thead>
<tr>
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<th>2014</th>
<th>2015</th>
<th>2016</th>
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<tbody>
<tr>
<td>NMO (2013)</td>
<td>15</td>
<td>17</td>
<td>30</td>
</tr>
<tr>
<td>MUSK+MG (2013)</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Wilson's Disease (2013)</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>HES/Leukemia (2015)</td>
<td></td>
<td></td>
<td>95</td>
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<td>195</td>
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Wilson’s Disease Registry

- 2014 ASFA Plenary Abstract Session
- J Clin Apher 2015 (Accepted for Publication)

This first report demonstrated the value of using this registry to collect apheresis-related patient outcomes from multiple centers. Study showed that TPE could be used to bridge WD patients to liver transplant - with six months survival of all 10 patients.
This second report demonstrated that overall subjective improvement was seen up to 94% of patients after one course of TPE. Five TPE may be adequate for initial course with additional TPE as needed. Some were non-responders.
This third report demonstrated that HES, used at low doses during leukapheresis procedures, was not associated with adverse events previously ascribed to its use as a volume expander. Study was a response by ASFA to a black box warning/banning of HES in Europe. An idea started in winter/fall of 2015!
Publications/Presentations

NMO Disease Registry

• 2015 ASFA Oral Plenary Abstract
  • Pending initial accrual by August 2017 for initial evaluation
Major Challenges

Funding
- Lack of intramural/extramural funding with the exception of REDCap secure database (CTSA grant through NIH)
- Lack of incentives!

Clinical staff support
- Dedicated CRAs for gathering data vs. busy allied health staff
- IRB applications/continuing reviews

Statistical support
- No dedicated statistical service

IRB approach
- Single, Focused vs. Multiple (General) Registry Approach
- Lack of Familiarity with Conduct of Research
Major Challenges

Research Approach (Getting Started!)

- Retrospective vs. Prospective Observational Studies
  - General data collection vs. specific data collection
- Comparison to a cohort?
- Biorepositories!???
Expanded Committee Structure

Hematology Related Subcommittees
- TTP/TMA
- Sickle Cell Disease
- Heparin Induced Thrombocytopenia

Disease/Condition To Be Studied
- Oncology (HES)
- Sickle Cell Disease
- Adverse Events
- Diseases - ECP
- Oncology (HES)

Non-Hematology Related Subcommittees
- Renal/FSGS
- Other Solid Organ Transplant/ABOi Liver
- Neurological Diseases NMO/MUSK+MG
- Nursing/Allied Health

Education/Communication/Funding
- Extramural Funding/Newsletter/Website Subcommittee

Joint subcommittee with Allied Health
- Joint subcommittee with Applications
Subcommittees/Chairs

Organ/Disease Specific

- Hematology/TTP (J. Raval/J. Kiss)
- Heparin Induced Thrombocytopenia (T. Onwuemene)
- Renal Disease/FSGS (K. Davis/C. Yamada)
- Neurological Disease/NMO/MUSK+MG (T. Ipe, S. Morgan)
- Adverse Events (E. Meyer, awaiting completion of the peds data)
- Oncology/HES Leukemia (M. Pagano)
- Solid Organ/ABO incompatible Liver Transplant (M. Pagano)/Wilson’s Disease (H. Pham)
- Sickle Cell Disease (H. Kim/Q. Eichbaum)
- ECP (J. Schneiderman/R. Edelman)
- Allied Health (M. Strunk)

Extramural Funding/Newsletter/Website

- T. Ipe, S. Thibodeaux, S. Joshi, E. Wong
Hematology Related Subcommittees Projects

- **TTP/TMA Subcommittee (biorepository proposed)**
  - Effect of taper type (gradual vs. complete stop) on relapse
  - Type of replacement fluid type on relapse
  - Effect of plasma volumes exchanged on relapse

- **Heparin Induced Thrombocytopenia Subcommittee**
  - **Primary Objective**
    - To create a comprehensive database of patient outcomes in HIT treated with TPE
  - **Secondary objectives**
    - To determine the efficacy of TPE for decreasing HIT-related complications
    - To determine the safety of TPE when used to treat HIT
    - To establish the optimal treatment parameters of HIT TPE treatment
  - **Long-term goal**
    - Multi-institutional randomized prospective trial of TPE for acute HIT

- **Sickle Cell Disease Subcommittee**— currently in discussion
Non-Hematology Related Subcommittee Projects

- **FSGS Subcommittee (biorepository proposed)**
  - Effect of TPE timing (prior/post transplant)

- **Neurological Disease (NMO, MUSK+MG)**
  - Complete data entry of approximately 30 additional NMO patients so that approximately 50 patients TPE treatments and outcomes can be analyzed

- **Adverse Events**
  - Awaiting completion of pediatric patients prior to adoption of REDCap database entry for adult patients

- **Oncology/HES**
  - Paper published regarding effect on renal function of acute leukemia patients undergoing WBC reduction in the absence or presence of HES
  - Ongoing discussion of future directions
Non-Hematology Related Subcommittee Projects

Solid Organ Transplant (non-renal)/Wilson’s Disease
- Continue data collection/ongoing discussion future directions for Wilson’s Disease
- Write review paper and practice survey on TPE in progress for ABOi liver transplant (M. Pagano/Q. Eichbaum) – followed by registry on outcomes

ECP (prospective observational study with biorepository) – with Applications
- To collect and analyze of patient information undergoing ECP at multiple treatment centers.
- To provide a repository for long-term storage of patients’ peripheral blood and collected mononuclear cells following, and addition of 8-methoxypsoralen (8-MOP) and photoactivation.

Allied Health (with Allied Health)
- Study outcomes related to additional blood filter during apheresis procedures.
Conclusions

ASFA Disease Registry

- Successful tool to foster multi-institutional collaborations among ASFA members to not only examine apheresis outcomes in WD, NMO, MUSK+MG, and HES/Leukemia, but also in the future other apheresis indications.
- Has allowed ASFA to successfully fulfill one of its research priorities (ie. publish a research manuscript based on the data collected in the apheresis registry)
Conclusions

ASFA Disease Registry

- Current efforts have been slow in several original registries primarily due to a variety of logistical and resource allocation reasons.
- Future continued efforts will likely require additional resources for continued success and participant recruitment
  - Research grant to improve infrastructure – in progress.
Questions?