The National Eye Institute: Patient Safety at the CC—Right Path?

Clinical Center Research Hospital Board
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Elizabeth Wendell, BSN, MS
Brian P. Brooks, MD, PhD
Outline

• Overview of the NEI Clinical Research Program
  • Organization
  • Research

• PDS Closure and the NEI

• Creating an environment of efficiency and safety
Mission Statement

Conduct high-quality research on the pathogenesis and treatment of blinding diseases in adults and children, while providing expert clinical care in a safe environment.
The Clinical Milieu

- Almost exclusively outpatient
- >9000 visits per year
- Close to 3000 of visits are consultations from other ICs
  - Clinical Care
  - Research collaboration
- Relatively light use of central CC resources (radiology, laboratory, etc.)
Who We Are...

• Six principal investigators (tenure track + tenured)
  • Two new Lasker Scholars
• Seven staff clinicians, one staff scientist
• Major research areas
  • Medical retina
  • Ocular immunology
  • Ophthalmic genetics
A Matrix Organization

Physicians

Clinical Director

Chief of Operations

Clinical Center Leadership

Nursing

Front desk
A Matrix Organization

• Advantages
  • Allows nimble management of limited resources across multiple investigators in real time
  • Allows for functional redundancy
  • Allows for sub-specialization of support staff

• Disadvantages
  • “Fragmentation of authority and responsibility for clinical operations” as cited as a potential pitfall by the Red Team
  • NEI solutions to this: Betsy Wendell will cover
Monitoring and Regulatory Affairs

• Two opportunities for improvement cited in Red Team Report
  • “Insufficient expertise in regulatory affairs”
  • “Insufficient regular monitoring and metrics”

• EMMES Contract Research Organization
  • Relationship established by Scott Whitcup, MD, previous Clinical Director
  • Protocols assigned appropriate levels of regulatory guidance and monitoring at time of scientific review
  • NEI-wide “Activation Meeting” for all intervention protocols; CC staff invited, participate
  • Clinical Center nursing invited to monitoring visits

• Data Safety and Monitoring
  • External DSMB for monitoring “large” interventional trials
  • Internal SAE Review Committee for quarterly group review of NEI SAEs
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Human Microbiome In Uveitis

- The pathogenesis of most forms of non-infectious uveitis remains a mystery
- Role for microbiome
  - Pathogenesis of autoinflammatory disorders (e.g., rheumatoid arthritis)
  - Data from animal models

Scatter plot showing a difference in the microbiome of Controls vs. Patients with Uveitis
Phase I/II study of oral minocycline in the treatment of GA associated with AMD

- Geographic atrophy (GA)
  - Leading cause of untreatable blindness in the developed world
  - Immune cells (microglia) implicated in pathogenesis
- Microglial activation modified by minocycline
  - Translation directly from Wong lab’s work showing microglial activation worsens retina degeneration
- Repurposes an approved oral medication
  - Unlikely to have been pursued by Pharma
iPS cell-derived RPE for AMD

• Authentic, autologous retinal pigment epithelium (RPE) derived from induced pluripotent stem cells (iPSCs)
• Developed transplantation technique in house
• IND Submission September 2018
• Made possible by CC Cell Processing Unit
  • David Stroncek, MD and Harvey Klein, MD
X-linked retinoschisis (XLRS) gene replacement therapy

- Affected boys develop schisis cavities in the neural retina
  - Acuity ~20/50-20/200
  - Macular atrophy by middle age
- scAAV8-hRS1/IRBP-hRS1 clinical vector
  - Preclinical efficacy in mouse model
  - Intravitreal injection
  - Phase I/IIa dose escalation

Images & data courtesy of Paul Sieving, MD, PhD

Electroretinogram showing improved response with therapy
Adaptive optics

• Allows for imaging of individual cells (rods, cones, RPE) in the living human subject
  • Longitudinal
  • Health and disease

• Clinical outcome variable at cellular resolution

• Understanding pathogenesis of disease (structure + function)
Effects of the PDS Closure on NEI Clinical Research

• Randomized placebo-controlled study of minocycline for geographic atrophy (AMD)
  • No placebo
  • Protocol redesigned to be open-label with run-in following the natural growth of GA
  • Delay 11 months to initiation

Wai T. Wong, MD, PhD
Effects of PDS Closure on NEI Clinical Research

- Randomized, placebo-controlled clinical trial of minocycline in branch- and central retinal vein occlusion
  - No placebo
  - These are acute events, no option for a run-in phase, followed by open label treatment
  - Required outsourcing of placebo from 3rd party
  - Delay > 2 years
  - Extra IC cost of >$30K
Effects of PDS Closure on NEI Clinical Research

• Gamma-interferon for macular edema in enhanced S-cone syndrome (ESCS)
  • Aliquoting investigational product into droperettes
  • Difficulties in having a workable beyond-use-date
  • Outsourcing cost-prohibitive
  • Study suspended indefinitely

Wadih Zein, MD and Sheldon Miller, PhD
Effects of PDS Closure on NEI Clinical Research

• Likely several projects never pursued because no clear path forward without a viable PDS
  • Effect on morale

• **The Good News**
  • Leadership of Dr. Majid Tanas, greatly improved communication
  • Monthly operations meeting between pharmacy staff and the NEI staff, CRO

• A path forward?
  • If one service previously offered by the PDS could be restarted, having the ability to create a matched oral placebo in house would be a tremendous positive step for the NEI clinical research program
Creating an environment of efficiency and safety

Elizabeth (Betsy) Wendell, BSN, MS
Clinical Operations Planning Meeting

• Established and overseen by William O’Donnell, Chief, Clinical Operations
• Weekly meetings to evaluate the clinical and research activities within the OP 10 and Op 11 clinics.
• Interdisciplinary membership represent all facets of the Institute and Clinical Center

• Goals
  • Escalate quality and safety concerns quickly
  • Communication across disciplines
  • Check-in with each discipline
  • Facilitates group decision making
  • Forum for rapid cycle change
  • Build consensus surrounding mission

Management
Support for Patient Safety

90%

2017 Culture of Safety Survey

Xueyang (Sharon) Yin, COA
Entering room to perform ERG
Daily Nursing Huddles

- Daily nursing huddles focused on daily clinical and research activities
  - Staff led
  - Review plan for high risk patients
  - Resource utilization
  - Just in time education
  - Announcements
  - Morale

- Safety and quality concerns with the goal of quick escalation.
Mini-360 : The Reasons Why...

• Perceived by senior NEI OCD leadership. Developed and implemented by Dr. Elizabeth C. Murphy Dep. Chief, Clinical Operations
• Knowledge is power
• Hard data are the starting point for recognizing strengths and weaknesses
• Knowledge and self-awareness are themselves sometimes agents of positive change
• Provides a metric for tracking progress
• The processes of both can be modified based on experience
• Nursing experience
Mini-360 continued...

- Dropdown menu of personnel
- Four axes
  - Research mission (includes attention to detail)
  - Patient care (includes medical/technical proficiencies, relationships with patients)
  - Communications
  - Teamwork
- Four “grades”: Outstanding, Very Good, Adequate, Needs Improvement
- Free text
Results

• Total 650 responses

2. Rate the individual on a scale of Needs Improvement, Adequate, Very Good, or Outstanding in the following areas. Please provide details in Comments for any area rated “Needs Improvement”.

- Research Mission (includes attention to detail)

- Patient Care (includes medical/technical proficiency, relationships with patients)

- Communication

- Teamwork

Total: 650
Thoughts

• This was an experiment
• Provides baseline
• Single negative comments should be taken as simply that; patterns are more important
• Plan
  • Repeat around Thanksgiving with closure around Christmas
  • Given to supervisors as one datum for performance assessments in January 2019
Ongoing and Future Directions

- **Research**
  - Interdisciplinary planning with new protocols
  - Increased ongoing participation at the activation meetings
  - Interdisciplinary monitoring visit-ongoing

- **Patient Care**
  - Revisions of standards of care of procedures performed in clinic
  - Use of primary nursing
  - Joint education days for patient care (NEI/CC staff)
  - Pharmacy collaborative

- **Communication**
  - NEI Town Hall Meetings
  - Dissemination of information

- **Team work**
  - Clinic Redesign
  - Monthly morale boosters
  - Daily planning

OP10 Team
Improving patient quality and safety: Intravitreal Injection

- Interdisciplinary planning
- Revision of standards of practice
- Focus on infection control
  - Centralization of sterilization
  - Review of procedures
- Focus on comfort during procedures
  - Equipment
  - Medications
  - Primary nursing

Rochelle Woodard, BSN, RN
Senior Clinical Research Nurse
Retina Protocol Coordinator
DID YOU RECEIVE EDUCATION REGARDING THE INDICATION OF MEDICATIONS ADMINISTERED?

WERE THE SIDE EFFECTS OF ADMINISTERED MEDICATIONS EXPLAINED?

WERE YOUR ALLERGIES REVIEWED DURING YOUR CLINIC VISIT?

DID YOU HAVE CONFIDENCE AND TRUST IN THE PHYSICIAN STAFF?

DID THE NURSES LISTEN CAREFULLY TO YOU DURING YOUR CLINIC VISIT?

DID THE NURSES DO EVERYTHING POSSIBLE TO CONTROL YOUR PAIN?
Consult Services: Quality and Safety

• We care for close to 3,000 consult patients per year
• Many patients are high risk
• Collaboration and communication
• Addition of 1.0 FTE for a consult primary nurse

Celestina Igbinosun, BSN, RN
Lieutenant, United States Public Health Consult Nurse
Celebration of Our Team

NIH Clinical Center won an excellence award in 2017 from the NRC Picker Institute for providing extraordinary high level of emotional support to our patients.

Thank You