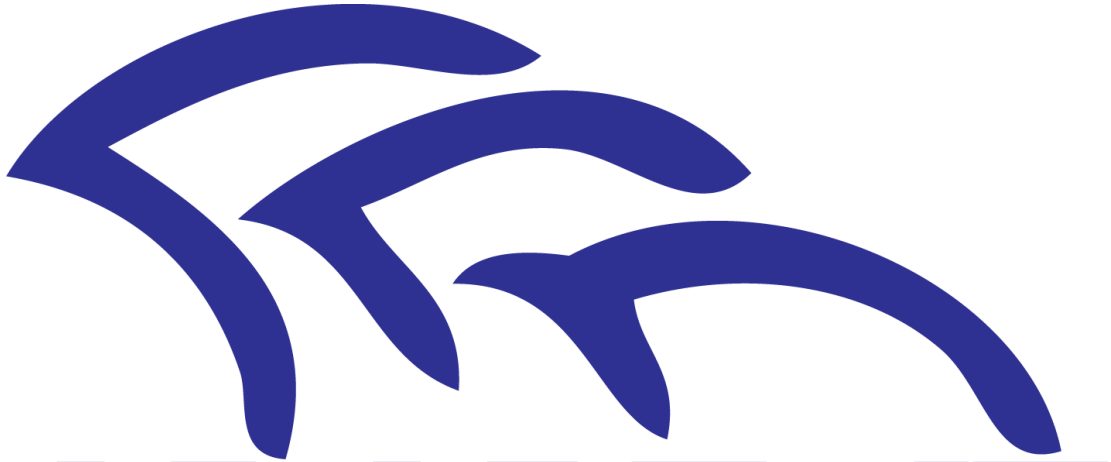

ADAPT–IT

Adaptive Designs Accelerating Promising Trials into Treatments

Supported by U01NS073476 with funds from the NIH Common Fund and the FDA

University of Michigan Health System

MUSC MEDICAL UNIVERSITY of SOUTH CAROLINA

LABioMed Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center

Berry Consultants Statistical Innovation

NIH - FDA

- Joint RFA for “Regulatory Science Innovation”
- 4 funded proposals
  - ADAPT-IT
  - Replacement Ocular “Battery”
  - Nanoparticle-complement interaction modeling
  - Heart-lung “Micromachine”

ADAPT-IT Investigators

- Principal Investigators
  - William Barsan, MD; University of Michigan
  - Donald Berry, PhD; MD Anderson/Berry Consultants, LLC
  - Roger Lewis, MD, PhD; Harbor-UCLA Medical Center
- University of Michigan
  - Shirley Frederiksen, BSN, MS
  - William Meurer, MD, MS
  - Robert Silbergleit, MD
- Mixed Methods Evaluation Team
  - Mike Fetters, MD
  - Laurie Legocki, PhD
- Berry Consultants
  - Scott Berry, PhD
  - Kristine Broglio, MS
  - Jason Connor, PhD
  - Michelle Detry, PhD
  - Todd Graves, PhD
  - Kert Viele, PhD
- Medical University of South Carolina - Data Coordination Unit
  - Yuko Palesch, PhD
  - Valerie Durkalski, PhD
  - Jordan Elm, PhD
  - Wenle Zhao, PhD
  - Ramesh Ramakrishnan, PhD

ADAPT-IT - Objective

- *"To illustrate and explore how best to use adaptive clinical trial designs to improve the evaluation of drugs and medical devices and to use mixed methods to characterize and understand the beliefs, opinions, and concerns of key stakeholders during and after the development process."*

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Specific Tasks

- Design ~~four~~, five clinical trials
  - Refractory seizures
  - Glycemic control in stroke
  - Hypothermia after spinal cord injury
  - Hypothermia after cardiac arrest
  - Progesterone for ischemic and hemorrhagic stroke

- Learn about process
  - Surveys
  - Focus Groups
  - Observation
  - Key Stakeholder Interviews
  - Thematic analysis

- Educate
  - Clinicians
  - Statisticians

FDA – NIH – Academic

- Unique, in that FDA expert biostatisticians are involved early and throughout the design process
- NIH program officials from NINDS – Clinical Trials are invited to all meetings

FDA Participants (partial)

- CDER
  - Sue Jane Wang, PhD
  - Robert O'Neill, PhD
- CDRH
  - Gregory Campbell, PhD
- CBER
  - Estelle Russek-Cohen, PhD

NIH Participants (partial)

- NINDS
  - Scott Janis, PhD
  - Robin Conwit, MD
  - Danilo Tagle, PhD

Laboratory - NETT

Neurological Emergencies Treatment Trials

Funded by NIH – National Institutes of Neurological Disorders and Stroke

- High stakes diseases
- Treatments must start in field or ED
- Open network
- Track record of successful trial implementation

ADAPT-IT Process

FTF - 1
- Investigators and statisticians meet
- Discuss clinical problem and potential designs

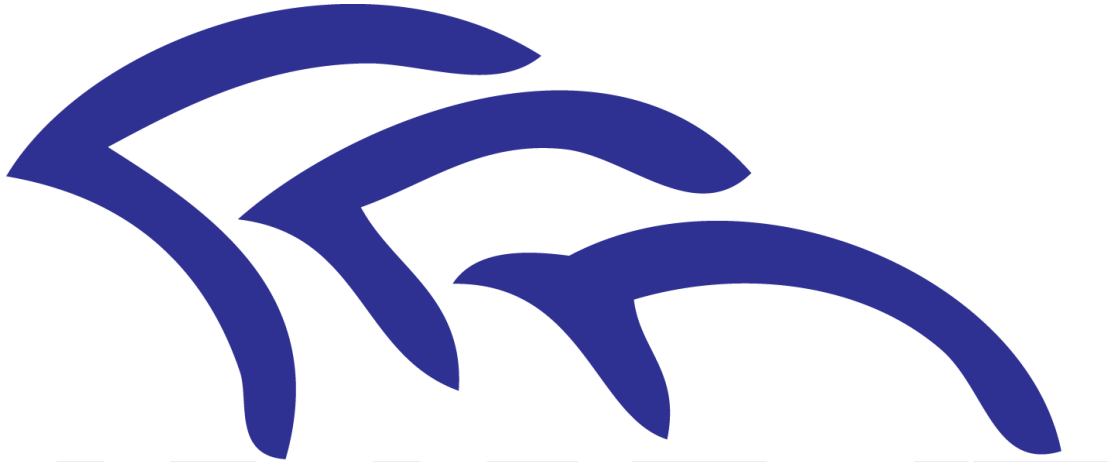
CTC
- Berry Consultants present concept
- Clinical & data teams provides feedback

Perf WG
- Simulations presented with feedback
- Several iterations

FTF – 2
- Near final design presentation
- Work out final details for grant / IND submission

Trial Status

Trial	Current Status
SHINE	Enrolling, multi-look frequentist interim analysis
ARCTIC	Completing resubmission of trial with ADAPT-IT design
ESETT	Completing 1st submission with ADAPT-IT design
ICECAP	Completing 1st submission with ADAPT-IT design
ProSPECT	Preparing 1st submission with ADAPT-IT design



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