Clinical Investigation of Neurological Channelopathies (CINCH) Landmarks

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CINCH Landmarks

- Patient-reported outcomes: interactive voice response system for
  - NDM
  - Periodic paralysis
  - Cardiac arrhythmias

- Clinical trial in NDM (Richard Barohn)
- Clinical Trial in the periodic paralysis, Andersen-Tawil Syndrome
- Training Program
  - 22 Fellows
  - 4 medical Students
- 16 additional grants for CINCH studies
- 94 publications
The effect of this episode on your daily function was:
1 Mild
2 Moderate
3 Severe

Are you experiencing an attack right now?
Yes

The average severity of the attack as you look at the visual scale was:
0-9

Do you want to report another episode?
Yes

The maximum severity of the attack as you look at the visual scale was:
0-9

If you are experiencing fainting please contact your cardiologist or primary care physician if you have not done so. Please call back when your episode has ended.

Thank you for calling Goodbye

END
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Phase II Therapeutic Trial of Mexiletine in Non-Dystrophic Myotonia (IND #77,021; 1R01-FD003454)

- Principal Investigator: Richard J. Barohn, MD, Co-I: Yunxia Wang, M.D. University of Kansas Medical Center
- FDA Orphan Drug Division - Funding: May 2008 - April 2011
  - 3 years total $949,028
- 60 patients; randomized, placebo controlled crossover study
  - NDM subjects from Natural History Study
  - 4 wks on mexiletine or placebo; 1 wk washout; crossover
  - 1° endpoint - patient report of stiffness on IVR (interactive voice response)
  - 2° endpoints - quantitative myotonia, electrophysiologic tests,
- DTCC data management and biostatistical support
  - Funded by NINDS supplement to CINCH - 1st meeting 5/28/08
- Study initiation meeting Oct. 25 Tampa, FL
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Examples:

(1) Mexilatine in nondystrophic myotonia
(2) Potassium/acetazolamide in the periodic paralysis Andersen Tawil syndrome
(3) Bringing dichlorphenamidine to registration for periodic paralysis – with Taro Pharmaceuticals
Taro funded by MDA to bring Dichlorphenamid to Market

- PAG (Periodic Paralysis Association) – President Jacob Levitt works for Taro
- MDA has awarded funding ($1 million) to enable Taro Pharmaceuticals U.S.A., Inc to provide DCP commercially to patients with the periodic paralyses.
- Taro has purchased the NDA from Merck
  - Will develop a synthetic method for the manufacture of pharmaceutically pure DCP to 2008 standards.
  - Will develop a formulation in which DCP is sufficiently bioavailable
  - Will perform clinical studies to establish bioavailability of DCP
  - Rochester will support the clinical arm of the project and provide safety and outcome data necessary for FDA filings
- Plan to bring the drug to the marketplace soon after the Phase III trial is complete.
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“Pivotal Studies of Orphan Drugs Approved for Neurological Diseases.”

Authors: J Mitsumoto (CINCH medical student), ER Dorsey, CA Beck, J Thompson, T Nguyen, K Kieburtz, RC Griggs

Comparing orphan drugs with non-orphan drugs
“Orphan drugs for neurological diseases have been approved by the FDA without randomized, doubled-blind, placebo-controlled clinical trials. As therapeutic development for orphan diseases is increasing, the design of alternative clinical studies will likely become more important.”


E. Matthews and the CINCH Investigators: Non-dystrophic myotonia. (In preparation for submission to Brain.)