Current Myositis Trials

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Myositis Trials

No longer enrolling

- Rituximab in Myositis
- Etanercept in Dermatomyositis
- MEDI-545 in Dermatomyositis and Polymyositis

Currently enrolling

- Lithium in IBM
- Arimoclomal in IBM
- Etanercept in IBM
- Stem Cell Transplant in Myositis
- Stem-cell transplant in children with refractory autoimmune disorders

Rituximab in Myositis

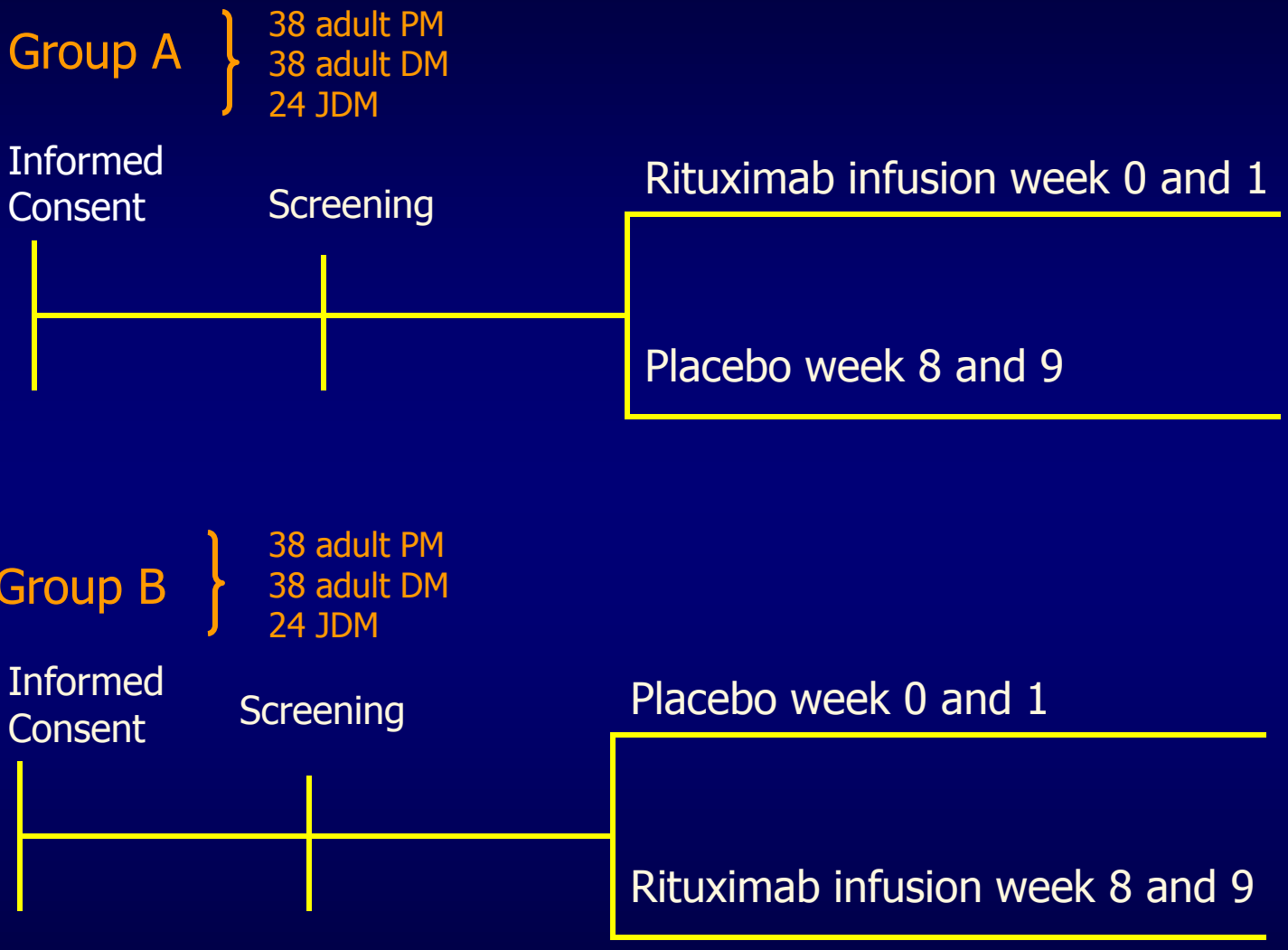
Rituximab in the Treatment of Refractory Adult and Juvenile Dermatomyositis (DM) and Adult Polymyositis (PM)

University of Pittsburgh, Coordinating Center
Dr. Chester Oddis, Principal Investigator

Why Use Rituximab in Polymyositis and Dermatomyositis?

- This antibody targets antibody producing immune cells (B cells)
- Eliminates B cells from the body
- It has been used in many different "autoimmune" diseases in both adults and children with encouraging results

Study Design



Primary Endpoint

The primary endpoint of this trial is to compare the time to achieve improvement between the two groups of rituximab-treated patients

Assumption: those patients receiving drug first (Group A) will get better sooner than those receiving the drug 8 weeks later (Group B)

Participating Centers: RIM Study

Adult Sites

- UAB, Alabama (Fessler)
- Harvard University (Narayanaswami)
- UCLA (Weisman)
- Stanford University (Chung)
- Czechoslovakia (Vencovsky)
- UT Southwestern, Dallas (Olsen)
- University of Kansas (Barohn/Latinis)
- University of Kentucky (Crofford)
- Mayo Clinic (Ytterberg)
- University of Miami (Sharma)
- University of Michigan (Seibold)
- MSU, Grand Rapids (Eggebeen)
- Medical College of Wisconsin (Cronin)
- North Shore, New York (Marder)
- NYU, New York (DiMartino)
- NIH (Miller)
- University of Pennsylvania (Kolasinski)
- Phoenix (Levine)
- Pittsburgh (Oddis/Ascherman)
- Sweden (Lundberg)

Pediatric Sites

- Harvard University (Kim)
- University of Cincinnati (Lovell)
- Duke University (Rabinovich)
- London (Pilkington)
- Mayo Clinic (Reed)
- Miami (Rivas-Chacon)
- MSU, Grand Rapids (Eggebeen)
- Creighton University, Nebraska (Jung)
- NIH (Rider)
- Halifax, Nova Scotia (Huber)
- University of Pennsylvania (Sherry)
- University of Pittsburgh (Kietz)
- Stanford University (Sandborg)
- Toronto (Feldman)

RIM Summary

- Largest multicenter study planned in myositis to date
- 200 subjects have been enrolled *(enrollment completed)* – 76 PM, 76 DM, 48 JDM
- 14 protocol visits over 45 weeks
- Initial results likely reported in Fall, 2010

A Pilot Study of Etanercept in Dermatomyositis

Brigham and Women's Hospital
Dr. Anthony Amato, Principal Investigator

Etanercept in Dermatomyositis

- Why use etanercept for dermatomyositis?
  - TNF is pro-inflammatory
  - TNF is over-expressed in DM muscle
  - Etanercept blocks tumor necrosis factor-alpha (TNF-alpha)
  - Etanercept has been used with success in other autoimmune diseases
    - Rheumatoid arthritis
    - Psoriasis
  - Case reports suggest it may effectively treat myositis

Etanercept in DM: Study Design

- Double-blind
- Placebo controlled (3/4 patients get etanercept 50 mg SQ/wk)
- 14 month duration; 16 outpatient study visits

Etanercept in DM: Outcome measures

- Primary
  - Safety and tolerability of treatment
  - Cumulative dosage of prednisone used during study period
- Secondary
  - Average daily dose of prednisone
- Assumption
  - If etanercept works, patients receiving it should use less prednisone

Etanercept in DM

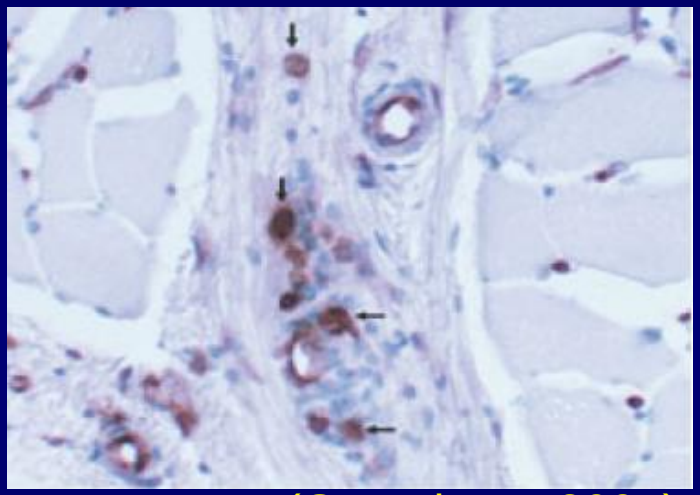
- 16 subjects enrolled
- No longer recruiting
- Will be completed by May, 2010
- Results available shortly thereafter

MEDI-545 in Dermatomyositis and Polymyositis

Sponsored by MedImmune

Why MEDI-545 for myositis?

- Interferon (IFN) plays a role in myositis
  - Myositis muscle contains cells that are potent sources of IFN



(Greenberg, 2005)

  - Type I IFN is increased in myositis muscle
  - Patients treated with Type I IFNs for other diseases can develop myositis
- MEDI-545 neutralizes IFN!

MEDI-545 in DM and PM

- Primary objective: safety and tolerability of MEDI-545
- Secondary objective: pharmacokinetics
- Exploratory objectives
  - Disease activity
  - Effect of drug on IFN levels in blood, skin, and muscle
  - Effect of drug on tissues (e.g., auto-Ab levels)

MEDI-545 in DM and PM: Study design

- Multicenter (~20 sites; ~32 patients)
- Randomized
- Double-blind
- Placebo-controlled (drug:placebo = 3:1)
- Dose escalation (starting with low doses and increasing if tolerated)

MEDI-545 in DM and PM

- Enrollment complete
- Results available…?

Lithium in IBM

- Currently Enrolling
- Enrollment = 20 patients
- Observational study
- Start 300 mg /day
  - p-tau accumulates in IBM muscle
  - GSK plays a key role in developing p-tau
  - Drug decreases GSK activity
- Phoenix Neurological Associates, LTD
  Contact: Nicole C Hank
  - 602 258 2432
  - nhank@pnal.net

Arimoclomal in sIBM

- Currently Enrolling
- Enrollment = 12 patients
- Randomized, double-blind, placebo controlled
- 100 mg three times/day for 4 months
- Drug activates the heat shock response
- University of Kansas Medical Center
- Contact: Dr. Richard Barohn
  - 913-588-6094
  - rbarohn@kumc.edu

Etanercept in IBM

- Currently Enrolling
- Enrollment = 30 patients
- Randomized, double-blind, placebo controlled
- 50 mg SQ/week x 12 months
- Washington University
- Contact: Dr. Glenn Lopate
  - 314-362-6981
  - lopateg@neuro.wustl.edu

Stem Cell Transplant in Myositis

- Currently Enrolling
- Enrollment = 10 patients
- Open-label, uncontrolled
- High dose cytoxan & ATG, then transplant
- Northwestern University, Feinberg SOM
- Contact: Dr. Dzemila Spahovic
  - 312-908-0059
  - d-spahovic@northwestern.edu

Stem-cell transplant in children with refractory autoimmune disorders

- Currently Enrolling
- Enrollment = 20 patients
- Open label
- Irradiation, cytoxan, ATG, then transplant
- Fred Hutchinson Cancer Research Ctr.
- Contact: Dr. Carol A. Wallace
  - 206-987-4448
  - cwallace@u.washington.edu

For Clinical Trial Information:

www.ClinicalTrials.gov