Dose-Toxicity Study of Oral Prednisone in Ocular Myasthenia

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Background

- Goals of therapy
  - Restore clear state of vision
  - Reduce the risk of progression to GMG

- Absence of data


- Clinical equipoise

  - Need to balance potential efficacy against potential for steroid side effects
The Controversy

- Do the benefits of steroids outweigh the risk of steroid therapy?
- Do ocular symptoms impair QoL or cause functional limitations?
- How effective is pyridostigmine?
- How effective are steroids?
- How frequent/severe are steroid side effects?
Study Design

- Enroll patients with newly diagnosed OM
- Treat with pyridostigmine x 1 month
- Randomize those whose symptoms fail to remit to one of two steroid dosing strategies
- Aggressive prophylaxis and treatment of steroid side effects
- Steroid treatment x 6 months
- Titrate steroid dosage against symptoms
- Quantify impact of symptoms & Rx on QoL
Specific Aims

- To select a tolerable steroid dosing strategy for an efficacy study
- To demonstrate the adverse impact of ocular symptoms on QoL
- To validate the ocular-QMG as an outcome measure
- To estimate the proportion of subjects whose ocular symptoms remit
Inclusion Criteria

- Weakness confined to extra-ocular muscles, levator or eye closure
- At least one abnormal diagnostic test
- Inadequate prior pyridostigmine treatment (dose not titrated to efficacy or intolorability)
- Age > 18; male or female
- Identifiable internist (to manage steroid AEs)
Exclusion Criteria

- Steroid treatment (> 10mg/day x 30 days)
- Current immune suppression
- Prior thymectomy
- Contra-indication to steroids (e.g. poorly controlled diabetes, HTN, glaucoma)
Outcome Measures

Primary

Ability to remain on prednisone for study duration without the occurrence of an adverse event that does not resolve with appropriate therapy or dosage reduction

Secondary

Quality of Life - INQoL

Ocular-QMG- reliability & validity

Subjective global impression of change

Time to MM & to ocular-QMG score of 0
Relevance to Efficacy Study

- Selection of tolerable prednisone dosing strategy
- Demonstration of impact of ocular symptoms and treatment on QoL
- Validation of ocular-QMG as outcome measure
- Enrollment/recruitment feasibility
Discussion

- Is the problem at important one?
- Is prednisone the best therapeutic choice?
- Is it worth studying two prednisone dosages?
- Phase II → III versus phase II/III
- Collaborative opportunities
  - Collect QoL data
  - Subject eligibility & willingness