International Consensus on the Conduct and Reporting of Myositis Clinical Studies

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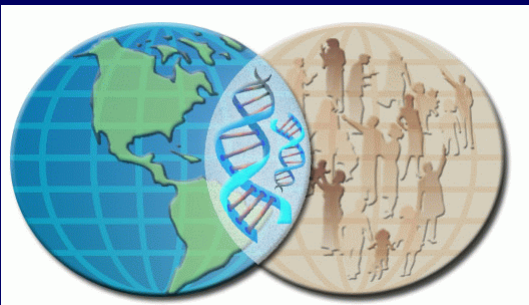

IMACS Approaches

Initial discussions among the executive group to review the literature, define overall goals, priorities, timelines and approaches

Executive group draft proposals that were discussed at planning meetings via Delphi methods and F/U email discussion/vote by IMACS

Face-to-face meetings using Nominal Group Technique (NGT) to assess certain problems and resolve difficult issues

Subsequent iterations of Delphi discussions and votes by email followed by additional face-to-face NGT meetings as needed

Iterative processes, sometimes data-driven and sometimes opinion-driven

NOMINAL GROUP TECHNIQUE - 1

- What is it?
  - **Structured group meeting to arrive at a group consensus about the answer to a question**
  - **Examples:**
    - **Should the inverse of the definition of clinical improvement be used for the definition of clinical deterioration?**
    - **Should adults and children be studied in separate or combined trials?**

NOMINAL GROUP TECHNIQUE - 2

- Advantages
  - **More focused discussion compared to traditional (free for all) meetings.**
  - **Greater flow of ideas compared to traditional mtgs.**
  - **Allows for equal participation of all members of the group (lessens dominance of the discussion by more senior or more vocal individuals).**
  - **Strong feeling of closure at the end of the meeting and satisfaction on the part of participants.**

NOMINAL GROUP TECHNIQUE - 3

- How do you do it?
  - Issues are careful defined prior to the meeting
  - Maximum number in each group is about 15.
  - A neutral, non-voting group leader introduces each issue and leads the group in a comment period - each participant is given equal time ~ 1-2 min for comments.
  - Anonymous vote by each participant of the issue at hand.
  - Counting of votes to determine if a consensus (~66-80%) has been achieved.

NOMINAL GROUP TECHNIQUE - 4

- The group leader will record on an overhead the responses for each issue if consensus has been achieved.
- If consensus is not achieved on that issue, the process is repeated.
- After the 2nd discussion, a 2nd vote is held to determine if consensus can then be achieved.

IMACS IIM Disease Activity Core Set of Measures

- Physician Global Activity: VAS or Likert scale
- Patient/Parent Global Activity: VAS or Likert scale
- Muscle Strength: MMT (proximal, distal & axial muscles)
- Physical Function: validated measure
  - HAQ
  - 2 tools recommended for children < 4 years of age
- Laboratory: Serum activity of ≥ 2 muscle enzymes
  - CK, LD, aldolase, AST, ALT
- Extra-Skeletal Muscle Disease Activity
  - Myositis Disease Activity Assessment (MyoAct, MITAX)

Miller, Rider et al., 2001, Rheum., 40: 1262-73

IMACS Desired Properties of Assessment Tools

- Practical – easy to use in multicenter international studies
- Reliable – reproducibly result in same measurements by the same rater over time and among different raters
- Applicable to all forms of myositis in both adults and children
- Validated
  - Face = sensible approach which capture attributes of interest
  - Content = comprehensively measure all important elements
  - Convergent construct = correlate with established standards
  - Discriminant = sensitive to change and can discern between active agents and placebos

Top Preliminary DOIs for Myositis Similar to ACR 20 for Rheumatoid Arthritis

Preliminary DOI Based on 6 Core Set Measures	***Sum(0–65)/ Rank***	***Sensitivity/ Specificity***
1. 3 of any 6 improved ≥ 20%, no more than 2 worse by ≥ 25%, which cannot be MMT	**57/ 1**	**83%/ 98%**
2. 3 of any 6 improved ≥ 20%, no more than 2 worse by ≥ 25%	**53/ 2**	**83%/ 98%**
3. 3 of any 6 improved ≥ 20%	**34/ 3**	**83%/ 98%**
4. MD global improved > 30% and MMT improved 1 – 15%, OR MMT improved > 15% and MD global improved > 10%, no more than 2 worse by ≥ 25%	**17/ 4**	**96%/ 85%**
5. 3 of any 6 improved ≥ 15%, no more than 1 worse by ≥ 25%, which cannot be MMT	**15/ 5**	**94%/ 80%**

IMACS Selected References

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2 Rider L; Giannini E; Harris-Love M; Joe G; Isenberg D; Pilkington C; Lachenbruch P; Miller F (2003). Defining clinical improvement in adult and juvenile myositis. *J Rheumatol* 30: 603-17.

3 Isenberg DA, Allen E, Farewell V, Ehrenstein MR, Hanna MG, Lundberg IE, Oddis C, Pilkington C, Plotz P, Scott D, Vencovsky J, Cooper R, Rider L, Miller F (2004). International consensus outcome measures for patients with idiopathic inflammatory myopathies. Development and initial validation of myositis activity and damage indices in patients with adult onset disease. Rheumatology (Oxford). 43(1): 49-54.

4 Rider LG, Giannini EH, Brunner HI, Ruperto N, James-Newton L, Reed AM, Lachenbruch PH, Miller FW. (2004) International consensus on preliminary definitions of improvement for adult and juvenile myositis. Arthritis Rheum 50 (6):2281--2290.

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