Developing A Disease Activity And Therapeutic Response Index In Connective Tissue Disease Related Interstitial Lung Disease: Results From A Delphi Exercise

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Disclosures

Actelion Pharmaceuticals US  Genentech
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Baxter         MedImmune
BMS               Novartis
Boehringer-Ingelheim  Pfizer
Bristol Myers Squibb  Sanofi-Aventis
Celgene           Sigma Tau
Ergonex         UCB
Fibrogen      United Therapeutics

Rationale

• Significant Morbidity / Mortality
• No ‘Approved’ or ‘Licensed’ Therapies
• New Therapeutics
• Lack of Reliable / Valid Measures
• No Consensus in Measurements of:
  • Disease Activity
  • Therapeutic Responsiveness
• Drug Development and Acceptance

Objective

• Obtain Expert Consensus
• To Identify Domains
• To Identify Instruments to measure identified domains
• Comply with OMERACT filter:
  • Truth
  • Discrimination
  • Feasibility
• Collect Comparative Data in CTD-ILD and IPF

Methodology

OMERACT: Outcome Measures in Rheumatology

Patient Perspective

Patient Focus Groups  On-Line Survey  Patient Perspective Results

Expert Delphi

Identify Experts And Measures  Three Voting Rounds  Expert Consensus Results

Nominal Exercise Consensus Summary
OMERACT: Outcome Measures in Rheumatology

Identify Experts And Measures

Patient Focus Groups

On-Line Survey

Patient Perspective Results

Nominal Exercise

Consensus Summary

Expert Consensus Methodology

- Invitations to ~270 experts in ILD
- Identified by peer review articles, specialist societies
- 248 Experts Agreed to Participate
- Core working groups of lead pulmonologists, rheumatologists, pathologists, radiologists assembled for stewardship over items of expertise
- Identify Domains and Measures that are important and useful in a 1 year multicentre RCT
- Comparative voting in IPF and CTD-ILD

The Delphi Process

- 150 Respiratory, 94 Rheumatology, 4 Cardiology, 5 Radiologists, 5 Pathologists (254 total)
- 74% - Interstitial Lung Disease as Primary Field of Interest
- 248 Voting Participants 36 Countries, 6 Continents

Consensus Identified

Preliminary Guidelines


CTD-ILD and IPF Brainstorm: Tier 0

248 Experts Built Survey

Tier 1

Tier 2

Tier 3

Consensus Identified

Preliminary Guidelines

Phase Yielded Analysis Method Domains CTD-ILD / IPF Instruments CTD-ILD / IPF Percent Participant Recidivism
Tier 0 Intense Review 23 616/616
Tier 1 ≤4 median cut-off 21 71/71 2%
Tier 2 cluster analysis 13 55/61 ≤1%
Tier 3 cluster analysis 5/5 under investigation 0%

Cluster Analysis – Data Reveals Optimal Analysis

9 Cluster s

5 Cluster s

3 Cluster s

Table 1 Results of Delphi Tier 3 Analysis of Domains

<table>
<thead>
<tr>
<th>Domains Name</th>
<th>CTD-ILD (median/mean)</th>
<th>IPF (median/mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>8.0/7.8</td>
<td>8.0/8.1</td>
</tr>
<tr>
<td>Health Related Quality of Life</td>
<td>8.0/7.7</td>
<td>8.0/7.8</td>
</tr>
<tr>
<td>Lung Imaging</td>
<td>9.0/8.3</td>
<td>9.0/8.3</td>
</tr>
<tr>
<td>Lung Physiology / Function</td>
<td>9.0/8.7</td>
<td>9.0/8.7</td>
</tr>
<tr>
<td>Survival</td>
<td>8.0/8.2</td>
<td>9.0/8.4</td>
</tr>
</tbody>
</table>

Domains Hierarchy Post Tier 3

Research Agenda

To Be Determined by Nominal Exercise

Core Domains 5
Next Steps
- Analysis of ‘Instruments’ from Delphi
- Pool Patient Perspective and Expert Delphi Results
- Nominal Group Technique with expert panel including patients, rheumatologist, pulmonologists and radiologists
- Preliminary Guideline for use in Clinical Trials

Conclusion
- First comprehensive, multi-disciplinary, international effort to assess domains for study of ILD.
- Development of valid, discriminatory and feasible outcome measures to assess disease progression and therapeutic responses is essential for performing RCTs in CTD-ILD.
- Broad participation from a multidisciplinary ILD research community reflects the high perceived need in this area.
- A research agenda focusing on candidate biomarkers and domains requiring instrument development has emerged.

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Thank You

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