Novel Methods Leading to New Medications in Depression and Schizophrenia (NEWMEDS) Consortium: Lessons Learned on Improving Efficiency of RCT’s on antipsychotic treatments

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NEWMEDS

Novel Methods leading to New Medications in Depression and Schizophrenia

One of the largest ever research academic-industry collaboration projects.

**EFPIA companies:** H Lundbeck A/S, Abbott, AstraZeneca AB, Eli Lilly and Company Ltd, Janssen Pharmaceutica NV, Novartis Pharma AG, Orion Corporation, Pfizer Limited, F. Hoffmann-La Roche AG, Institut de Recherches Servier

**Universities:** King’s College London *(UK)*, Karolinska Institutet *(Sweden)*, The University of Cambridge *(UK)*, Central Institute of Mental Health *(Germany)*, CSIC *(Spain)*, The University of Manchester *(UK)*, Bar Ilan University *(Israel)*

**SME’s**

Psynova Neurotech Ltd *(UK)*, deCODE genetics *(Iceland)*, GABO:mi *(Germany)*
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NewMeds Goal: Find new methods for development of drugs for schizophrenia and depression.

Today's presentation: Findings & lessons from NewMeds repository of antipsychotic randomized controlled trial (RCT).
Methodological Accomplishments

• We have established a consortium that shares clinical trial data –coded patient/participant level data-- from industry and academia to examine precompetitive questions.

• Overcome challenges associated with establishing data sharing

• Pooled and mined data from studies that have sufficiently common experimental designs to have a reasonable chance of valid conclusions.

Text borrowed from: Institute of Medicine, Washington, DC, August 2011, Cast as road map.
Schizophrenia Database

Data from: Astra Zeneca, Janssen, Lilly, Lundbeck, Pfizer

64 Industry sponsored studies
  34 placebo controlled
  30 active comparator
25,900 patients
  16,105 study drug
  7,119 active comparator
  2,676 placebo

1 NIMH sponsored study CATIE 1,493 patients
1 European Union sponsored study EUFEST 498 patients
Depression Database

Data from: Astra Zeneca, Lundbeck, Pfizer

26 placebo controlled Industry sponsored studies

8,053 patients
5,504 active drug
2,549 placebo

Additional data to arrive from Lilly.
Major findings

Placebo-controlled antipsychotic studies

• Efficacy results at 4 weeks almost the same as at week 6.
• Females show more pronounced differentiation from placebo than males, primarily driven by lower placebo effect in females.
• Patients with a later onset of disease show more pronounced improvements, irrespective of their allocation to active or placebo, but differentiation from placebo is not affected by age of onset.
• Patients age ≤ 30 with ≥ 4 years of illness show highest active vs. placebo differentiation.
• Patients with both prominent positive and negative symptoms show the most pronounced active-placebo differentiation.
• Impact of above characteristics contribute independently.
• Persons just meeting symptom eligibility criteria are not overrepresented but show a somewhat lower active-placebo differentiation than the rest of the study population.
• The use of benzodiazepines does not affect the treatment results, active-placebo differentiation.
• Active-placebo differentiation differs per geographical area, considerably more differentiation in Eastern Europe than North America.
Sample sizes needed per arm (90% power, p of .05)

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<thead>
<tr>
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<th>6 Weeks</th>
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<tr>
<td>Current studies</td>
<td>79</td>
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<tr>
<td>Current enriched</td>
<td>64</td>
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<tr>
<td>50% Female</td>
<td>71</td>
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<td>50% female enriched</td>
<td>60</td>
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<td>50% Early episode</td>
<td>57</td>
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<tr>
<td>50% Early episode enriched</td>
<td>53</td>
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<tr>
<td>50% Female &amp; 50% Early episode</td>
<td>52</td>
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<tr>
<td>50% F &amp; 50% EE enriched</td>
<td>46</td>
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Current=70% female; 20% early episode; 40% enriched
Enriched=prominent positive and negative symptoms
Note: Per patient cost 6wk study $70,000-$100,000
Implications of findings on future drug development

- Trials of 4 weeks duration.
- Representative / enriched populations, particularly in Proof of Concept trials.
- More efficient trial designs
- Data informed regulatory policy and new studies
- Paradigmatic shift: data sharing as ethical imperative

**Limitation:** Some findings may not be applicable for new compounds with different mechanisms of action.
Personal experiences
Facilitators

• Commitment of companies to partner with external funding around precompetitive challenges.

• Recognition by industry that drug discovery was becoming more difficult.

• Need for clear message, ongoing support from top
  – Ideal partner from top management.

• Previous relationships

• Peer pressure among companies

• Active collaboration regarding formulating research questions and interpreting data.
Challenges

- Locating data
  - Changes in corporate structure
  - Acquisitions
- Competing for internal resources and priorities
- Change in personnel
- Complexity of data storage, disparate systems
  - Differences within companies and between companies and over time.
- Data controllers and extent of cooperation.
  - Compartmentalization of companies.
- HIPA
- Concerns of legal departments
  - Ethical benefits of data sharing
Future

What if all trials were stored in a uniform way and patient level data routinely entered into data bank?

Who is best positioned to do this?

How does data sharing or un-willingness to share data impact the risk benefit ratio of conducting a study?

Our experience is that the common good can be greatly enhanced by sharing data.