Patient-Focused Drug Development and Patient-Centered Clinical Care: Working Together

A Case Study in Multiple Sclerosis
**Agenda and Workshop Panelists**

- **Introduction of Panelists and Workshop Topics**
  - Robert McBurney, PhD, Accelerated Cure Project & iConquerMS™ PPRN
- **Experience of MS and Treatment**
  - Federica Balzani, Dr. (Law), Italian MS Society
- **Patient-Centered Clinical Care and Patient-Reported Outcomes**
  - Giampaolo Brichetto, MD PhD, Clinical Director Rehabilitation Center, Italian MS Society
- **Patient-Focused Drug Development**
  - Schiffon Wong, MPH, Exec. Dir., Global Evidence & Value Development, EMD Serono
- **Audience Participation: Polls, Q&A and Contributions**

**Who is Participating in the Workshop? - Poll**

**RAISE YOUR HAND**

- Patient or patient representative
- Healthcare practitioner
- Med. specialty society representative
- Pharmaceutical company personnel
- Device company personnel
- Diagnostic company personnel
- Service/Analytical company personnel
- Academic/Institutional researcher
- Representative of regulators
- HTA Agency representative
- Insurance Co. representative
- Government payers personnel
- ISPOR representative/staff
- Media representative
- Other
Who has Experience in....?

RAISE YOUR HAND

- Patient-Focused Product (Drug, Device, Dx) Development
- Patient-Centered Clinical Care
- Patient-Reported Outcomes
- Clinician-Reported Outcomes
- Performance Outcomes
- Shared Treatment Decision-Making
- Clinical Decision Support Tools

Workshop Topics

Robert McBurney
Topics to be Addressed in the Workshop

- What symptoms, etc., affect or matter most to people with MS
- Does clinical care or drug development address the symptoms, etc., that matter most to people affected by MS?
- What can be done/learnt in the clinic to enable patient-centered care?
- How can patient-focused drug development be achieved?
- How patient-focused drug development can work with patient-centered clinical care to improve outcomes for people with MS?

What are We Trying to Achieve in MS?

Improved symptoms, abilities and quality of life for people in all areas of their experience of MS

How have you been since your last clinic visit?

.........

Patient Reported Outcomes (PROs) are important to people with MS, healthcare providers & healthcare companies

PROs complement Clinician-Reported Outcomes (ClinROs) and Performance Outcomes (PerfOs)
Impact Areas for Outcome Assessments

Future State

Outcome Assessments
- Patient-Focused Drug Development
- Clinical Trial Results

What is the Future?
- Working Together
- Improved Health, Healthcare & Quality of Life

Current Assessment of People with MS

Clinical Reported Outcomes
- Relapses (? Progressive MS)
- Neurological Exam
- EDSS?
- MRI Characteristics

Performance Outcomes
- Timed 25ft Walk
- 9-Hole Peg Test
- Single Digit Modalities Test
- Low Contrast Visual Acuity

PROMs*
- Landscape of Available Measures
  Khurana et al., Eur. J Neurol, 2017
- 8094 articles reviewed
- 1102 articles selected
- 405 PROs identified
- 323 non-MS-specific
- 82 MS specific

* Patient-Reported Outcome Measures
iConquerMS™: People-Powered Research Network bridged to Researchers and Other Stakeholders

- >4,600 registered participants, growing daily
- Established with funding from PCORI (PCORnet1.0)
- Governed by majority of PwMS - the experts
- Research portfolio developing rapidly

**OPEN SCIENCE driven by People with MS to accelerate MS research**

What Affects iConquerMS™ Participants Most?

<table>
<thead>
<tr>
<th>Rank Order</th>
<th>Neuro-QoL Domain (5-point Likert scale questions)</th>
<th>Average Score (N = ~1,400)</th>
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<tbody>
<tr>
<td>1</td>
<td>Fatigue</td>
<td>2.89</td>
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<tr>
<td>2</td>
<td>Satisfaction with Social Roles and Activities</td>
<td>3.09</td>
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<tr>
<td>3</td>
<td>Sleep Disturbance</td>
<td>3.59</td>
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<td>4</td>
<td>Positive Affect and Well Being</td>
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<tr>
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<td>Cognitive Function</td>
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All respondents as of May 2016
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The other symptoms and quality of life domains have rarely been available in MS clinical trial results and submissions.

Mobility is captured in the regulatory outcome measure Expanded Disability Status Scale (EDSS)\textsuperscript{1}

1. ClinRO

iConquerMS™ is Collaborating in 2 Related Areas

Harmonizing the collection and use of PROs in care and research across cultures

How can we bring the initiatives together to optimize their impact on the health, healthcare and quality of life of people affected by MS?
Experience of MS and Treatment

Federica Balzani

From Injectable Therapy to Oral Therapy
Symptom Domains that Matter to People with MS

- Fatigue
- Bladder dysfunction
- Walking and mobility
- Anxiety
- Depression
- Visual problems
- Hearing problems
- Pain
- Cognitive losses
- Ataxia and tremor
- Balance and falls
- Vertigo/dizziness
- Temperature sensitivity
- Sleep disturbances
- Speech difficulties
- Swallowing difficulties
- Emotionalism
- Spasticity and spasm
- Contracture at joints

Design with The End in Mind

MYTH: PROs are by definition patient-centered

REALITY: Not necessarily. Many PROs were developed with insufficient understanding about what matters to patients and inadequate partnership with patients in measurement development.

MYTH: If patients are reporting on an outcome, it matters to them.

REALITY: Many patients can be compliant with filling out surveys regardless of whether the questions resonate with what is important to them. PROMs can have adequate psychometric properties....yet still not capture outcomes that matter to patients.
MULTI-ACT and the Science of Patient Input

A Collective Research Impact Framework and multi-variate models to foster the true engagement of actors and stakeholders in Health Research and Innovation

Paola Zaratin, MULTI-ACT Project Coordinator on behalf of MULTI-ACT Consortium

WP1. THE SCIENCE OF PATIENT INPUT

OVERALL GOAL
Patients to become partners, key stakeholders, in the process of co-creation within the overall HEALTH Responsible Research and Innovation (RRI)

Innovative strategies, methodologies, tools for Patient Engagement (PE)
Measuring MS is a hard challenge mainly due to the variety of functional problems that may affect individual patients. A universally accepted measurement instrument that is precise, reliable, easy to administer, captures the key neurological domains affected by MS, is sensitive at various levels of disability and that accurately reflects neurological and neuropsychological disability is lacking.
Italian MS Society Foundation in 2013 promoted and funded the initiative:

“A new functional PROfile to MOnitor the PROgression of disability in Multiple Sclerosis” (PROMOPRO-MS).

There is consensus in the clinical and scientific community that not only the long-established Expanded Disability Status Scale (EDSS)\(^1\) (Kurtzke, 1983), but also the Multiple Sclerosis Functional Composite (MSFC)\(^2\) (Fischer et al., 1999) are inadequate to capture the change of the patients’ clinical condition (Cohen et al., 2012).

**PROMOPRO-MS: Key Questions**

What is a set of outcomes related to the functional domains that really matter to People with MS? 
**mobility, upper limb dexterity, fatigue, cognitive performance, emotional status, bladder continence, quality of life**

How do we validate a “functional profile” of MS based on meaningful variables and measures?

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**PROMOPRO-MS and Clinical Care**

The study is continuously collecting in a **real-life setting**, every four months, data from PwMS* followed at the Rehabilitation Centers of the Italian MS Society Foundation

- **ClinRO** • **EDSS** - Expanded Disability Status Scale
- **ClinRO** • **FIM™** - Functional Independence Measure
- **PRO** • **Abilhand** - (perceived manual ability in daily life)
- **PRO** • **OAB-Q** - Overactive Bladder Questionnaire
- **PRO** • **M-FIS** - Modified-Fatigue Impact Scale
- **PerfO** • **SDMT** - Symbol Digit Modality Test
- **PRO** • **MoCA** Questionnaire
- **PerfO** • **PASAT** - Paced Auditory Serial Addition Test
- **PRO** • **HADS** - Hospital Anxiety and Depression Scale
- **PRO** • **LSI** - Life Satisfaction Index

*No inclusion/exclusion criteria were considered apart from MS diagnosis as inclusion criteria*
The proposed set of outcomes is currently used to measure disease progression and the efficacy of treatments (drugs and/or rehabilitation) in a real-life clinical setting.
Meaningful, systematic consultation, involvement, and partnership with patients and their caregivers, will enhance the value of innovative medical products and improve the integration of therapeutics into the context of patients’ lives.

Roadmap to Patient-Focused Outcome Measurement in Clinical Trials

1. Understanding the Disease or Condition
   - A. Natural history of the disease or condition:
     - Onset/Duration/Resolution
     - Diagnosis
     - Pathophysiology
     - Range of manifestations
   - B. Patient subpopulations:
     - By severity
     - By onset
     - By comorbidities
     - By phenotype
   - C. Current Clinical Practice(s):
     - Clinical care standards
     - Treatment alternatives
     - Health care system (e.g. access to care)
   - D. Patient/caregiver/expert perspectives:
     - Definition of clinical benefit
     - Benefit-risk tradeoffs
     - Impact of disease

2. Conceptualizing Clinical Benefit
   - A. Identify concept(s) of interest for meaningful clinical benefit, i.e.,
     - How a patient:
       - Survives
       - Feels (e.g., symptoms)
       - Functions
   - B. Define context of use for clinical trials, for example:
     - Disease/Condition entry criteria
     - Clinical trial design
     - Endpoint definition
     - Endpoint positioning

3. Selecting/Developing/Modifying the Outcome Measure
   - A. Select clinical outcome assessment (COA) type:
     - Patient-Reported Outcome (PRO)
     - Observer Reported Outcome (ORO)
     - Clinician-Reported Outcome (CRO)
     - Performance Outcome (PerK)
   - B. Search for a COA measuring the concept of interest in context of use:
     - COA exists and is fit for purpose
     - COA exists but needs to be modified
     - COA under development
     - No COA exists (development needed)
   - C. Develop and Evaluate a COA:
     - Content validity
     - Reliability and construct validity
     - Ability to detect change
     - Interpretation of meaningful within patient change

Advancing the Science of Patient Input from Development to Decision Making

Source: Measuring what matters to rare disease patients – reflections on the work by the IRDiRC taskforce on patient-centered outcome measures

Transformative Collaboration: ACP/iConquerMS™ & EMD Serono

Patient-Focused Drug Development Council composed of Diverse People with Multiple Sclerosis

- Patient feedback on design of PRO endpoints* in MS clinical trials
  - Is there suitable coverage of domains most important to patients?
  - Is the timing of PRO assessments consistent with patient experience?
  - Identification of relevant aspects of patient experience to be assessed outside RCTs

- Patient feedback on results of PRO measures validation studies
  - Feedback on whether PRO measures reflect the patients’ voice.
  - Adding the patients’ voice to the way validation study results are reported and communicated

- Establishing criteria for interpreting PRO endpoints
  - Patient insights on clinical significance criteria for several PRO measures
  - Conceptualizing the magnitude of benefit patients would consider relevant for the investigational therapeutic

- Generate additional evidence/insights on MS disease burden
  - Co-generate research questions, which will be investigated with the iConquerMS™ patient-powered research network using mixed methods

*As a component of a mixed methods research program to support the development of PROs
Practical Considerations from Conceptualization to Execution

1. Joint brainstorming on potential scope
   See “eye-to-eye”

2. Search & identify partner
   Consider complementary interests, resources, & capabilities

3. Joint development of detailed scope
   Align on objectives, expectations, & define mutual benefits

4. Incorporate insights into decision-making program

5. Map internal stakeholders

6. Recruit representative patients
   Seek continuity rather than a transaction

7. Follow internal legal & compliance processes

8. Select program & identify priorities

Audience Participation:
Q&A and Contributions

Robert McBurney, Discussion Facilitator
How can Stakeholders make this a Reality?

Outcome Assessments
- ClinROs
- PROs
- PerfOs
- ObsROs

Patient-Focused Drug Development

Clinical Trial Results

Working Together

Clinical Practice

Clinical Care Data

Improved Health, Healthcare & Quality of Life

Workshop Questions

- From your stakeholder perspective, what are top priorities, or low-hanging fruit, for bringing together patient-centered clinical care and patient-focused product development?
  - Patient / Patient Representative
  - Product developer
  - Regulator
  - Healthcare technology assessor
  - Payer / Government
  - HEOR researcher
  - Medical specialty professional society
  - ISPOR
Workshop Questions

• What challenges are currently facing stakeholders in engaging with patients in patient-centered clinical care or patient-focused product development?

• What needs to be done to address the current challenges?

• What opportunities do you see for translating the patient perspectives and insights captured during drug R&D into patient-centric care in clinical practice?

Workshop 14

Patient-Focused Drug Development and Patient-Centered Clinical Care: Working Together

A Case Study in Multiple Sclerosis

Thank You