NAAF PATIENT-REPORTED OUTCOMES CONSORTIUM

Bringing the voice of the patient into the drug development process
OBJECTIVE

• develop a single, evidence-based patient-reported outcome measure for alopecia areata for qualification as a Drug Development Tool to support medical product approval and labeling claims
What’s driving focus on PRO & CER?

From Advisory Groups

- IOM 2001
- NRC 2011

From Within Us

- Human Genome Sequenced 2003
- Retail Genome and Whole Exome Sequencing for $99 - $499 in 2016

National Academies

- Toward Precision Medicine
- Healthy People 2010

US Department of Health and Human Services

- ODPHP 2000 and 2010
- AHRQ 2011

IOM 2001

NRC 2011

Healthy People 2020

AHRQ 2011
What’s driving focus on PRO & CER?

Legislation requiring increasing patient engagement, patient-centered outcomes and CER

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>Patient Drug User Fee Act (PDUFA)</td>
<td>PDUFA I: Backlog reduction</td>
</tr>
<tr>
<td>2008</td>
<td>PDUFA IV: Process for Engagement</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>PDUFA V: Benefit/Risk Biomarkers/PROs 20 public meetings</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>Patient Protection &amp; Affordable Care Act</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>Patient-Centered Outcomes Research Institute (PCORI): Investigate comparative effectiveness Inform Medicare coverage decisions</td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td>American Recovery &amp; Reinvestment Act</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Funding for CER</td>
<td></td>
</tr>
</tbody>
</table>

Funding for CER

PDUFA VI: Engagement throughout lifecycle

PDUFA V: Benefit/Risk Biomarkers/PROs 20 public meetings

PDUFA IV: Process for Engagement

PDUFA I: Backlog reduction

FDA

American Recovery & Reinvestment Act

Patient Protection & Affordable Care Act

Patient-Centered Outcomes Research Institute (PCORI):
Investigate comparative effectiveness Inform Medicare coverage decisions

BlueCross BlueShield

National Alopecia Areata Foundation
GAP ANALYSIS

• Three existing AA-specific PRO instruments
  • significant gaps in development per FDA PRO Guidance

• Available generic instruments
  • insufficient to support product labeling claims

• PDUFA VI enhances inclusion of patients
  • patient input throughout instrument development
INITIATIVE RATIONALE

• Shared investment and value
• Third-party neutrality
• Recognition and reach with patient community
• Patient engagement credibility with FDA
• Industry expertise navigating FDA
• Single standardized approach for eventual CER
AA PRO Consortium Partners

Alopecia Areata KOLs

Biopharma Industry Partners
### Timeline and Milestones

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Assemble Consortium Partners and select Working &amp; Observer Groups</td>
<td>Conduct 15 phone Interviews with adults recruited from clinical sites to elicit concepts of meaningful treatment benefit</td>
<td>Protocol Amendment with study procedures and interview guide</td>
<td>Prepare Qualitative Report</td>
<td>Develop Psychometric Statistical Analysis Plan (SAP)</td>
</tr>
<tr>
<td>DDT Tracking # FDA letter of intent CPIM Meeting 4/19</td>
<td>Transcribe and Analyze data</td>
<td>IRB Approval of Amended Protocol</td>
<td>Prepare Initial briefing package</td>
<td>Conduct Psychometric analyses</td>
</tr>
<tr>
<td>Kick-off Meeting – elicit constructs of interest to PRO Consortium</td>
<td>Content and Conceptual Framework including Preliminary PRO Instrument with instructions</td>
<td>Conduct 30 Interviews with Draft AA PRO Instrument</td>
<td>Consortium Progress Meeting</td>
<td>Prepare Final Validation Report</td>
</tr>
<tr>
<td>Develop Qualitative Study Protocol</td>
<td>Consortium Progress Meeting</td>
<td>Transcribe and Analyze data</td>
<td>Initial briefing package to FDA</td>
<td>Prepare Follow-up briefing package for FDA Submission</td>
</tr>
<tr>
<td>IRB Approval of Study Protocol (6/20/17)</td>
<td>Propose changes to PRO Instrument based on findings</td>
<td>Prepare Initial briefing package</td>
<td>Conduct Psychometric analyses</td>
<td>Consortium Progress Meeting</td>
</tr>
<tr>
<td>Conduct 15 adult and 10 adolescent in-person Interviews during NAAF Conference to elicit concepts of meaningful treatment benefit</td>
<td>Laying the groundwork &amp; Ongoing Communication</td>
<td>Review Protocol for PRO Validation – Test scoring, reliability and validity in current or recent clinical trial (timing depends on whether we can slot into an existing trial or do a stand-alone validation)</td>
<td>Follow-up briefing package to FDA</td>
<td>Prepare Abstract and manuscript for publishing</td>
</tr>
</tbody>
</table>

**PHASE I**
- Qualitative Study - Conceptualizing treatment benefit, Develop Draft AA PRO Instrument

**PHASE II**
- Quantitative Study – Test, Validate and publish AA PRO Instrument
PROCESS OVERVIEW

• Phase I (Concept Elicitation Interviews):
  • Identify important concepts related to AA and inform measure development.

• Phase II (Cognitive Interviews):
  • Assess content validity of the measure.

• Phase III (Validation):
  • Examine scoring structure, reliability and validity of the AA PRO.
PHASE I: RESULTS

• Interviewed 30 adults and 12 adolescents
  • recruited through NAAF as well as five clinical sites

• Results
  • single measure is appropriate for adults (≥ 18 years) and adolescents (12-17 years)

• FDA Engagement –
  • 2 CPIM calls with deep FDA bench.
  • Buy-in to concept of Kybella-like primary satisfaction question with additional clarifying questions.

• Key concepts identified:
  • hair coverage, hair quality and impacts related daily activities, coping and emotions

• Draft PRO Developed
PHASE II: PROGRESS

- Cognitive interviews in 20 adults and 10 adolescents
  - Adults: 18/20 interviews completed
  - Adolescents: 10/10 interviews completed

- Address quantitative properties of draft PRO, including:
  - clarity of the items
  - Interpretation of the items
  - ease of completion
  - comprehensiveness of the instrument
  - format, response scales, and recall period

- Refine PRO measure based on cognitive interviews
  - slot into clinical trials in Q1/Q2 of 2019
PHASE III: VALIDATION

• Psychometric evaluation of new PRO (scoring, reliability, validity) in planned clinical trial

• Review clinical protocol
  • recommend additional PROs to support construct validity
  • recommend assessment time points to document test-retest reliability
  • inform development of Psychometric Statistical Analysis Plan (SAP)

• Potential to submit for DDT qualification of PRO in adults and adolescents if validation includes both age groups
CHALLENGES & BENEFITS

CHALLENGES:
• BioPharma bureaucracy challenging and slow to navigate
• FDA months to schedule meetings or provide feedback

POTENTIAL BENEFITS:
✓ “Above Brand” industry collaboration to benefit patients
✓ Consistent instrument across trials for eventual CER
✓ Build relationships with FDA and educate them about aa