Advancing Patient-Centered Outcomes Research through Patient Partnerships

PCOR
Patient-Centered
Outcomes Research

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Value & Evidence

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Patient-Centered ≠ Patient Engagement

PATIENT-CENTERED

Broadly means any process, program or decision focused on patients in which patients play an active role as **meaningfully engaged participants,** and the central focus is on optimizing use of patient-provided information.[1]

PATIENT ENGAGEMENT

Active, meaningful, authentic, and collaborative interaction between patients and researchers across all stages of the drug development and commercialization process, **where decision-making is guided by patients' contributions as partners, recognizing their unique experiences, values and expertise[2]**

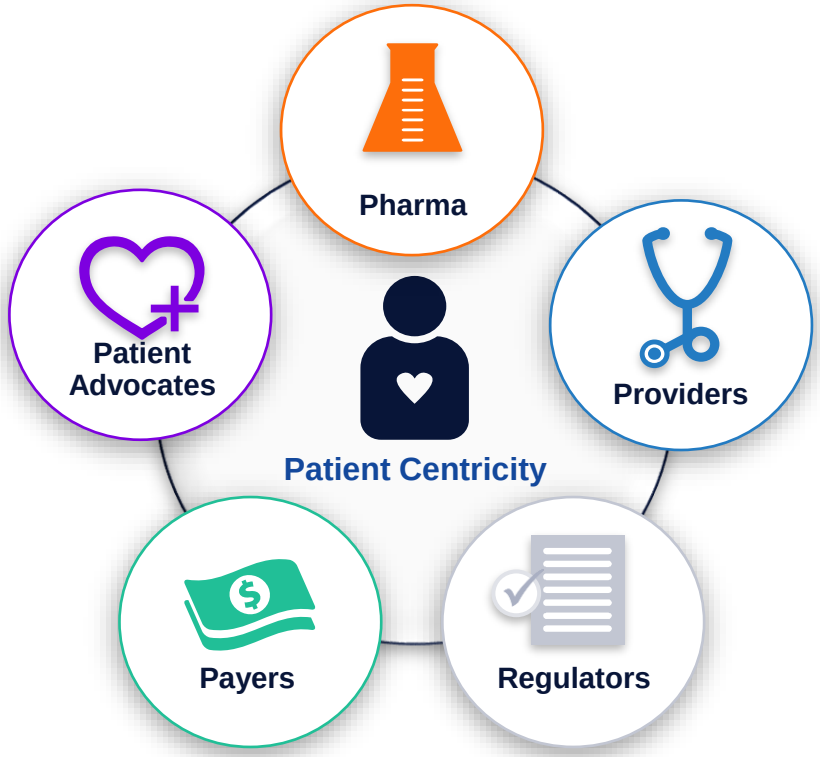
Patient engagement must be done with patient-centered approach to yield meaningful & reciprocal partnerships that are successful in driving impact for patients

1 NHC Patient Engagement Rubric, 2019
2 ISPOR PC-SIG, 2018

Growing Emphasis on Patient-Centricity in Healthcare Ecosystem

Rapidly Evolving Landscape

- Patients are recognized as the **ultimate decision-makers**
- Regulators are requesting **patient experience data to inform risk-benefit decision-making**
- Payers are demanding **demonstrated value** in cost-constrained environment
- Health care delivery systems are shifting to **value-based outcomes** and pay-for-performance
- **Increasing competition** for innovative drug development with focus on product differentiation



Aligning Medical Product Development with Patient Needs

Embedding the patient perspective into medical product development **enables comprehensive assessment of unmet needs & treatment benefit to inform healthcare decision-making** across stakeholders

Patients as Partners in the Drug Development Ecosystem

Evolving the historical model of “Subjects” > “Participants” > **“Partners”**

Guiding Principles

- Building and maintenance of relationships established on trust and respect
- Transparent and bidirectional information sharing
- Mutually beneficial partnerships

Levels of Engagement

*Importantly, **patient engagement** relies on:*

People + Relationships =

Not one size fits all

Relationships require:

Time + Effort + Care

Possess in finite quantities

openness, understanding, empathy, authenticity, patience, respect, honesty, collaboration

Initiating Patient Engagement

- What do you want to accomplish with patient engagement?
- How do I get started and with whom?
- What considerations should I be mindful of?

Potential Goals for Research Partnerships in PED Evidence Generation

What are you seeking patient engagement/insights for?

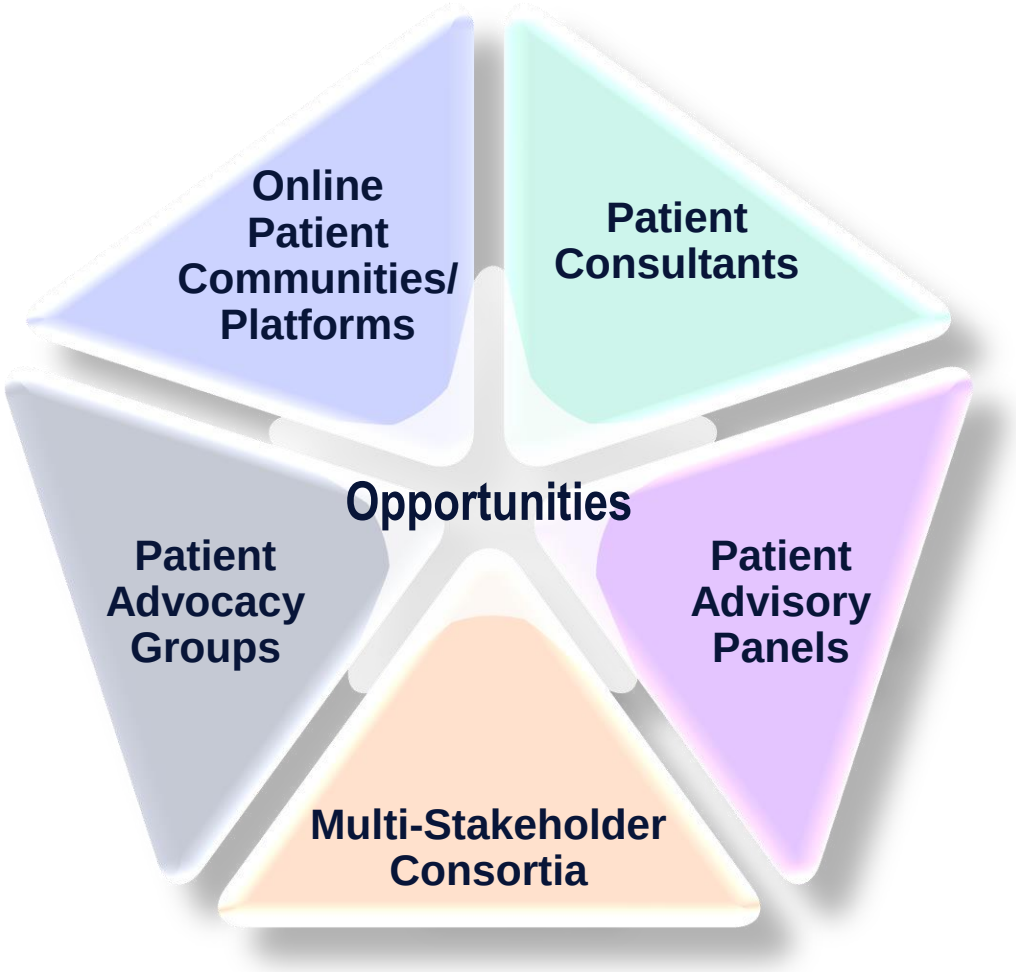
Early Patient Insights

- Understand disease/condition and patient population
- Identify concepts that matter to draft conceptual disease models
- Initial conceptualize of target COA measurement concepts
- Inform study design & protocols for PED research (e.g., interview guides; inclusion/exclusion criteria)

Patient-Centered Measure & Endpoint Development

- COA development research (e.g., co-creation of study materials; interpretation of results)
- Participation in COA development studies (e.g., CE, CD, exit interviews)
- Core outcome set development
- Recruitment support

Opportunities for Patient Partnerships in PED Evidence Generation



Collaborations with Patient Advocacy Groups

- Externally-led PFDD meetings
- Research partnerships and educational opportunities

Multi-Stakeholder Consortia

- Development of novel COA measures
- Collaborative research to document PED

Patient Consultants/Patient Advisory Panels

- Input on the concepts that matter most
- Co-creation of trial protocols and PED research protocols and interview guides
- Interpretation of findings

Incorporating the Patient Voice in Drug Development

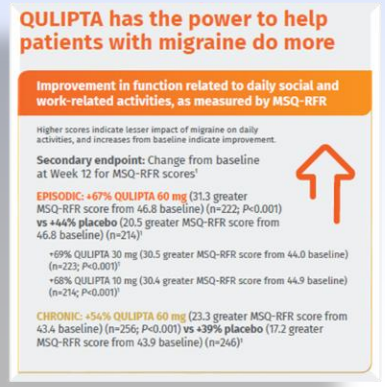
Patient engagement enables the identification and elevation of the **concepts that matter** in drug development

2021 & 2023[1]

1

Comprehensive Functional Improvements in Migraine

Elevated Patient Functioning as Key Differentiator for QULIPTA

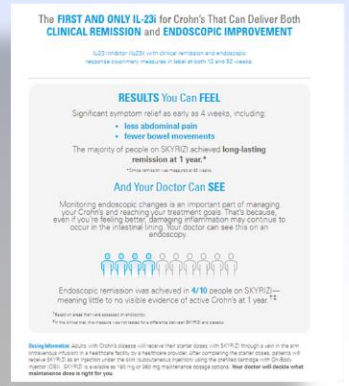


2022

2

CD Abdominal Pain & Stool Frequency

Substantiated SKYRIZI Efficacy in Improving Patient-Centric Symptoms



2022

3

PsA ClinRO Assessing Fingernail Psoriasis

Differentiated SKYRIZI on Key Patient-Centric Outcome

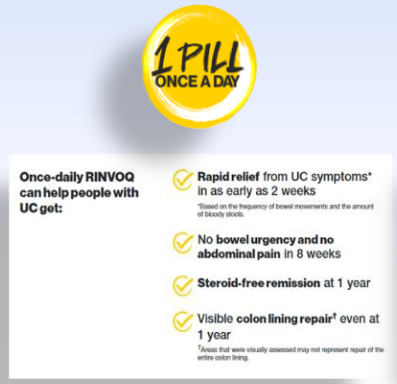
Pr Skyrizi® (risankizumab) injection

2022 & 2023[2]

4

UC Abdominal Pain, Urgency & Fatigue

Communicated Treatment Benefits on Novel Endpoints with RINVOQ



2023

5

Oral Treatment for CD with Fatigue

Elevated Impact of RINVOQ on Key Patient Symptom

2023

6

PRO Endpoints Support Approval for Pediatric FC Patients

Expanded LINZESS Indication to Pediatric Population

CD, Crohn's Disease; ClinRO, Clinician-reported outcome; FC, Functional constipation; PRO, Patient-reported outcome; PsA, Psoriatic Arthritis; UC, Ulcerative Colitis

1Initial approval in episodic migraine in 2021; indication expansion to chronic migraine in 2023

2Initial approval in 2022 included abdominal pain and urgency; label expansion in 2023 included approval of fatigue

QULIPTA: Assessing Treatment Benefit on Functional Improvement in Episodic & Chronic Migraine

Concept
(“Thing” measured)

Social and Work-related Activities

Performance of Daily Activities

Physical Impairment

Patient Informed

Instrument
(Tool to measure concepts)

Migraine Specific Quality of Life Questionnaire (MSQ v2.1)

Activity Impairment in Migraine – Diary (AIM-D)

Patient Informed

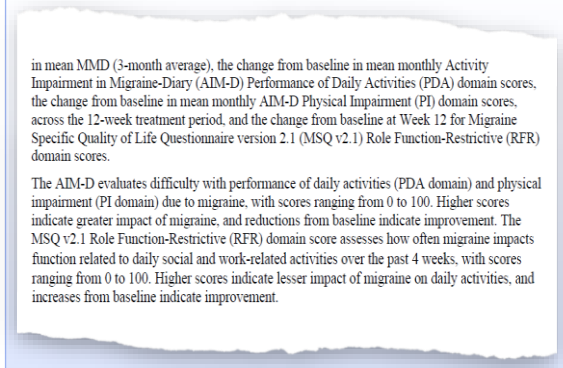
Endpoint
(Precisely defined variable based on instrument)

Key Secondary Efficacy Endpoint:

- Change from baseline in MSQ v2.1 Role Function-Restrictive domain score at Week 12
- Change from baseline in mean monthly Performance of Daily Activities domain score of the AIM-D across the 12-week treatment period
- Change from baseline in mean monthly Physical Impairment domain score of the AIM-D across the 12-week treatment period

Communication
(Documentation of treatment benefit)

Qulipta® Label (2021)



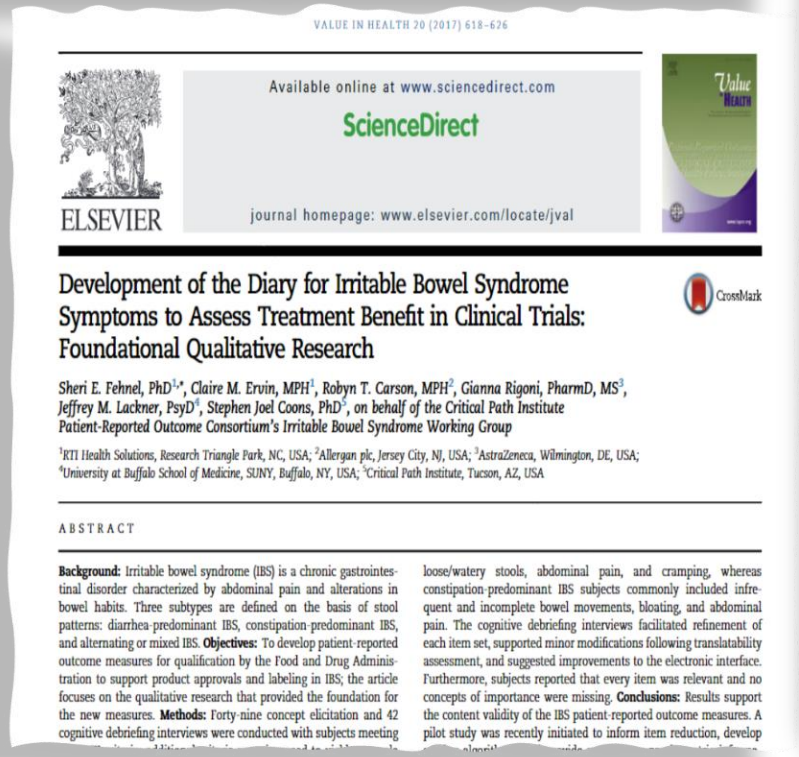
in mean MMD (3-month average), the change from baseline in mean monthly Activity Impairment in Migraine-Diary (AIM-D) Performance of Daily Activities (PDA) domain scores, the change from baseline in mean monthly AIM-D Physical Impairment (PI) domain scores, across the 12-week treatment period, and the change from baseline at Week 12 for Migraine Specific Quality of Life Questionnaire version 2.1 (MSQ v2.1) Role Function-Restrictive (RFR) domain scores.

The AIM-D evaluates difficulty with performance of daily activities (PDA domain) and physical impairment (PI domain) due to migraine, with scores ranging from 0 to 100. Higher scores indicate greater impact of migraine, and reductions from baseline indicate improvement. The MSQ v2.1 Role Function-Restrictive (RFR) domain score assesses how often migraine impacts function related to daily social and work-related activities over the past 4 weeks, with scores ranging from 0 to 100. Higher scores indicate lesser impact of migraine on daily activities, and increases from baseline indicate improvement.

Data to Inform Decision-making

Elevating the Patient Perspective in Development of Qualified COA:
Critical Path Institute PRO Consortium IBS Working Group

Elevating the Patient Voice through Identification of Concepts that Matter



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Development of the Diary for Irritable Bowel Syndrome Symptoms to Assess Treatment Benefit in Clinical Trials: Foundational Qualitative Research

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ABSTRACT

Background: Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterized by abdominal pain and alterations in bowel habits. Three subtypes are defined on the basis of stool patterns: diarrhea-predominant IBS, constipation-predominant IBS, and alternating or mixed IBS. **Objectives:** To develop patient-reported outcome measures for qualification by the Food and Drug Administration to support product approvals and labeling in IBS; the article focuses on the qualitative research that provided the foundation for the new measures. **Methods:** Forty-nine concept elicitation and 42 cognitive debriefing interviews were conducted with subjects meeting loose/watery stools, abdominal pain, and cramping, whereas constipation-predominant IBS subjects commonly included infrequent and incomplete bowel movements, bloating, and abdominal pain. The cognitive debriefing interviews facilitated refinement of each item set, supported minor modifications following translatability assessment, and suggested improvements to the electronic interface. Furthermore, subjects reported that every item was relevant and no concepts of importance were missing. **Conclusions:** Results support the content validity of the IBS patient-reported outcome measures. A pilot study was recently initiated to inform item reduction, develop

Updated PROs on Label

Trial 6 (NCT03573908) was a randomized, double-blind, placebo-controlled, parallel-group trial that evaluated the safety and efficacy of LINZESS in patients with IBS-C over a 12-week treatment period followed by a 4-week randomized withdrawal period. A total of 614 patients [mean age of 47 years (range 18 to 85 years), 81% female, 63% white, 24% black, and 27% Hispanic] received treatment with LINZESS 290 mcg or placebo once daily and all patients met Rome III criteria for IBS-C.

The efficacy of LINZESS was assessed using a primary endpoint based on the mean abdominal score (composite of abdominal bloating, abdominal discomfort, and abdominal pain) across 12 weeks. The secondary endpoint was a responder analysis based on at least a 2.5-point improvement in the abdominal score from baseline for at least 6 out of 12 weeks. See results in Table 5 and empirical Cumulative Distribution Function (CDF) plot in Figure 1.

Table 5: Efficacy Endpoints in IBS-C Trial 6: Overall Change from Baseline in Abdominal Score and Responder Rates for at Least 6 Out of 12 Weeks

	Trial 6		
	LINZESS 290 mcg (N=306)	Placebo (N=308)	Treatment Difference [95% CI]
Baseline Abdominal Score	6.4	6.5	
Least Squares 12-week Mean Change from Baseline in Abdominal Score*	-1.9	-1.2	-0.7 [-1.0, -0.4]
Abdominal Score 6 of 12-Week Responder**	33.3%	17.9%	15.5% [8.7%, 22.3%]

* Primary Endpoint, ** Secondary Endpoint
Each abdominal symptom was rated on a 0-to-10-point numeric rating scale where 0=no [symptom] and 10=worst possible [symptom].
CI = Confidence Interval

Amplifying the Patient Voice to Communicate Treatment Benefit

1. **Patient Input for COA Development Activities**
2. **Multi-stakeholder Effort including Patient Advocacy**
3. **Engagement & Alignment with FDA**

Diary of IBS Symptoms for Constipation qualified in Dec 2020, measuring key patient-relevant bowel & abdominal symptoms

*Granted qualification by the FDA for measurement of IBS-C symptom severity in December 2020 (https://www.fda.gov/drugs/clinical-outcome-assessment-coa-qualification-program/ddt-coa-000005-diary-irritable-bowel-syndrome-symptoms-constipation-dibss-c)
DIBSS-C, Diary for Irritable Bowel Syndrome Symptoms – Constipation; IBS-C, irritable bowel syndrome with constipation

Key Takeaways

- Meaningful patient engagement enhances the relevance & impact of patient-centered outcomes research; patients are the experts in their condition
- Direct engagement with patients is necessary to ensure:
  - Treatments that we develop directly address the outcomes that matter most to patients
  - Patient-relevant outcomes data are included as core evidence in regulatory & reimbursement decision-making
  - There is adequate information available for individuals to make informed treatment decisions for themselves & their families
- Be intentional & adaptable as every situation is unique