Patient engagement in Clinical Development
The role of Medical Affairs

Presented by the MAPS Patient Centricity Working Group and guest
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Educational objectives

Understand the benefit of engaging with patients throughout the medicine development lifecycle, starting early during the discovery phase with a specific focus on **Clinical Development**

Explore, **using case studies,** patient engagement in clinical development to understand disease burden, patient experience, unmet needs, and new treatment expectations to optimize clinical trial design including:

- Schedule of assessment
- PRO development / selection
- Patient preference studies

Highlight the **critical role of Medical Affairs** in initiating and developing patient partnerships at the clinical development phase to ensure effective long-term collaborations

Gain **awareness of resources and best practices** to facilitate patient engagement in clinical development

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The role of Medical Affairs in driving patient centricity across the product lifecycle

Introducing the webinar series

Introducing the webinar series

The role of Medical Affairs in driving patient centricity across the product lifecycle

Discovery

Webinar 1: Early discovery

- Understanding patient experience and unmet need
- Developing Target Value Profiles

Clinical development

Webinar 2: Clinical development

- Optimizing clinical trial design
- PRO development / selection
- Patient preference studies

Pre-launch / launch

Webinar 3: Communication and education

- Communication of clinical data
- Patient education materials
- Publications PLS
- Disease awareness programs

Post launch

Webinar 4: Real-world evidence generation

- Patient support programs
- Real-world studies, PROs etc
- Ongoing unmet needs

Polling question 1

What is your level of experience of patient engagement within the clinical development stage?

- I have no experience incorporating patient engagement in research
- In my company patients are involved in clinical development but Medical Affairs are not involved
- In my company Medical Affairs are involved in patient engagement throughout clinical development

Polling question 2

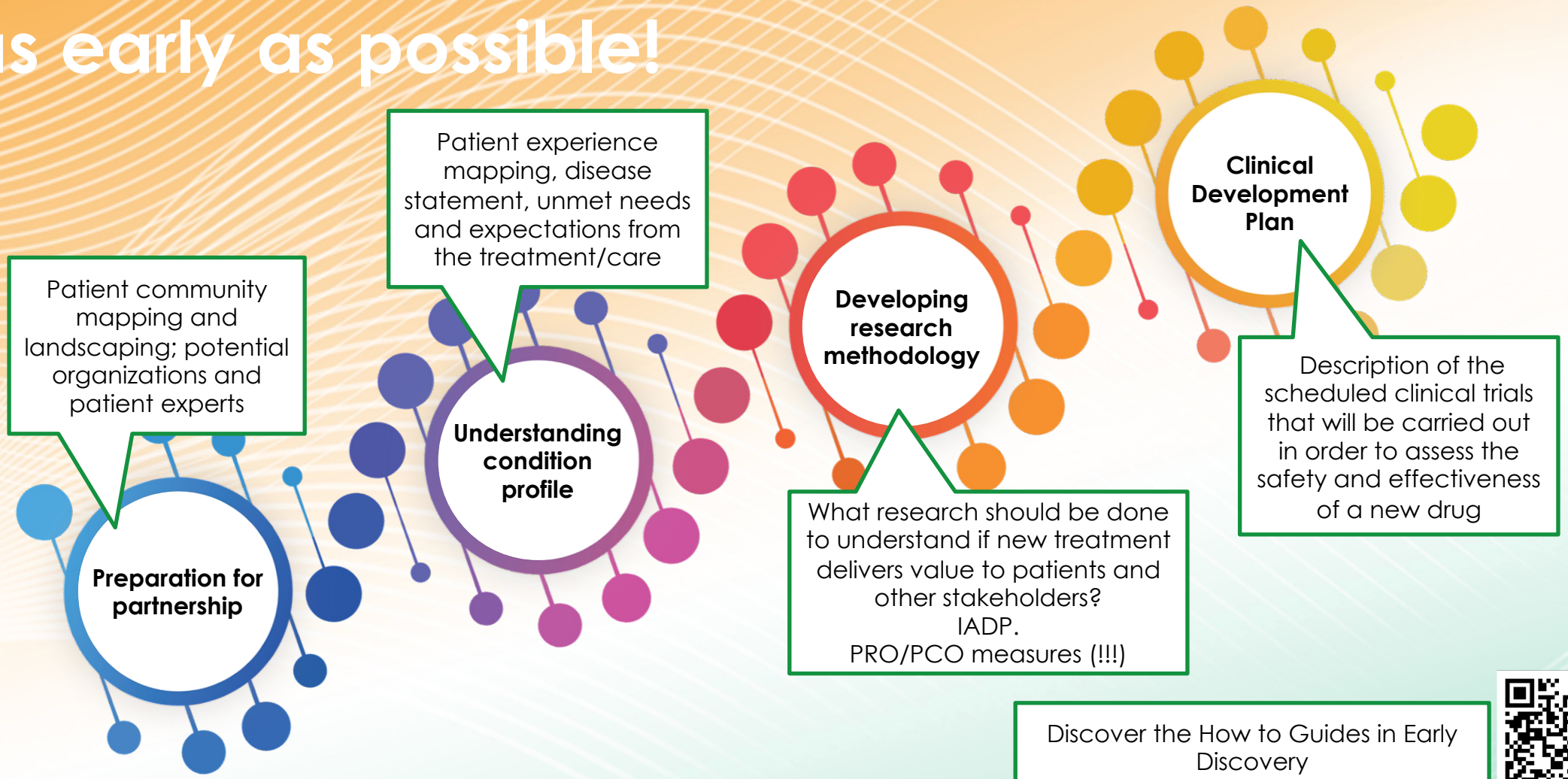
Do you agree that Medical Affairs should be involved in clinical development to coordinate engagement and facilitate advice-seeking and insights-gathering activities with patient experts?

- No – patient partners will add little value and prolong timelines
- Not really – patient input is important but this should be done by our colleagues in another function
- Yes – patient engagement throughout clinical development is useful and Medical Affairs are well placed to do this

Patient engagement in the clinical development phase: The role of Medical Affairs

Rebecca Vermeulen

Start as early as possible!



Discover the How to Guides in Early Discovery

Source: PFMD PEM Suite

This Guide has been co-created to:

- Allow for comprehensive guidance to be outlined in a single document.
- Compile information related to specific steps in the patient engagement process in sequential sections

Discover the How to Guide on PE in Clinical Trial Protocol Design

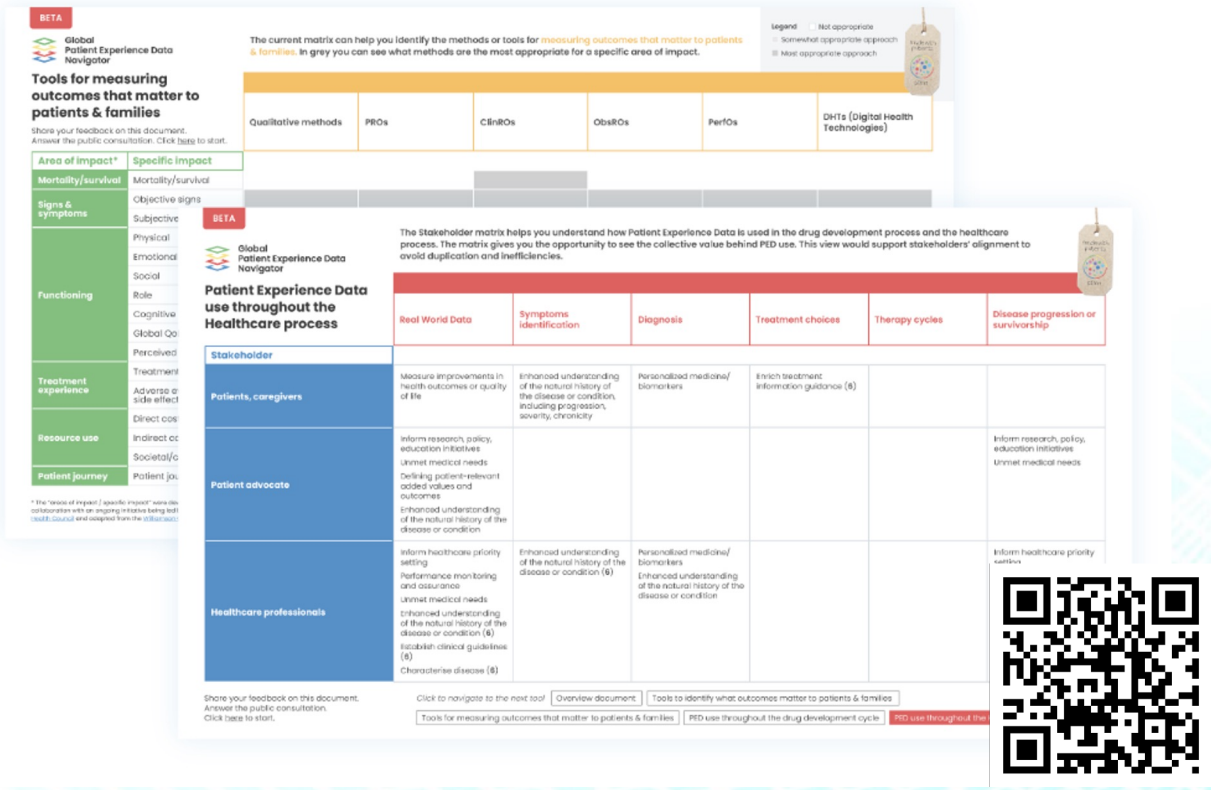
The Global PED Navigator responds to 5 key questions, resulting in 4 integrated templates, to add clarity and structure to PED

1. **WHAT:**
   Highlight the needs that are most important to patients

2. **HOW:**
   Review the approaches and methodologies available (and identify gaps) to measure these patient experiences

3. **WHEN:**
   Consider when stakeholders are using this data and **4. WHY**

5. **WHO:**
   Identify the stakeholders that are using PED



Source: PFMD PEM Suite

Lack of patient engagement in drug development results in lower value for all stakeholders, delayed patient access and higher societal costs

Patients face challenges throughout their treatment journey, and clinical trials today reflect a broken system

- 80% of trials fail to meet enrollment timelines
- Enrolled demographics are unrepresentative, affecting trust, equity and medical efficacy
- Historic exploitation continues to impact trust in trial operators. Willingness to participate in trials has dropped below 50%

Meanwhile Pharma is struggling to maintain R&D effectiveness amid evolving market dynamics

- Only ~10% of agents investigated in the R&D phase are developed and launched
- Pressure from institutions and payors to prove cost-effectiveness paired with a shift to value-based contracting where “income depends on outcome”
- 53% of launches have underperformed in the last 3 years while R&D spend across US pharma industry rose to $83 billion

Implementing Patient Inclusivity provides a variety of benefits

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- Integrating patient needs in R&D can enable more efficient recruiting of diverse patient populations, decreased dropout, and more meaningful endpoints
- Designing products and services to address unmet needs will accelerate diagnosis, drive earlier treatment starts, decrease never-starts, and increase adherence
- Tracking and measuring patient outcomes provides competitive advantage and the data to differentiate products and ensure favorable access and adoption
- Being an early mover in implementing organization-wide patient inclusivity will expand partnership capabilities and generate a strong goodwill with industry stakeholders
- Connecting employee contributions to patient outcomes can increase satisfaction, commitment and innovation

Opportunities to Add Value

Key Opportunities to Add Value - As Shared by the Patient Community

There are significant unmet needs not being addressed by industry across the different parts of the patient journey that are limiting optimal care

All unmet needs can be grouped into four key areas:

MEDICAL: Can refer to any clinical challenges faced by patients

EMOTIONAL: Can refer to hopes, fears and concerns around wider implications on quality of life

INFORMATION AND SUPPORT: Can refer to information, education and support (or lack of) provided to people with lived experience

ACCESS: Can refer to eligibility, location, reimbursement or physical accessibility

Key areas where value can be added to patients are:

Ensuring the right information is provided to patients and GPs

Improving patient – HCP interaction

Helping patients in tracking their symptoms to better manage their disease and ideally predict flares

Supporting patients with holistic care across other areas that may impact their lives, such as mental health

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Systematic Approach to Shape Clinical Development

Patient-Inclusive Trails in Clinical Development

Patient-inclusive trials are defined as

"Investigations that prioritize the needs of all patient at all stages, including design, activation, enrollment, data collection, completion and outcome reporting. In patient-inclusive trials, hypotheses that are important to all patients are formulated, studies are designed to minimize burden on all patients and measures implemented ensure that trial conduct and data generation are regulatory compliant and support potential improvement to the standard of care can be implemented."

Reimagining patient-centric cancer clinical trials: a multi-stakeholder international coalition. B.T. Li et al. Nature Medicine. 2022 Apr; 28:614–629.

A systematic approach to cover all aspects of clinical trials

Study

Development

Protocol development & amendment reviews

- Endpoints
- Eligibility criteria
- Patient-reported outcomes
- assessments

Community members embedded into study team to provide ongoing, real-time feedback

Community review of AE management strategy

Set-Up

Engage patient communities as part of country/site selection

Co-create tools and tactics around raising clinical trial awareness, participation, and engagement with the community

Engage the community to serve as expert speakers at investigator meetings

Conduct

Share materials with community leaders for use in responses to member inquiries

Discuss protocol design with community leaders to ensure support/helplines understand the details

Proactive use of community letters to engage with the worldwide patient community on priority topics

Engage with community leaders at conferences and congresses

Develop a continuous feedback loop with the community (with focus on regulatory and access strategy discussions)

Close Out

Collaborate with community in the development of lay person summaries

Partner with community on projects that address evidence gaps (e.g., Patient Preference Studies)

Case Study: aHUS Patient Community

Working with the Global aHUS Alliance, we have shaped studies early and systematically to…

Understand the impact of aHUS on patients' lives and community expectations of future treatment options

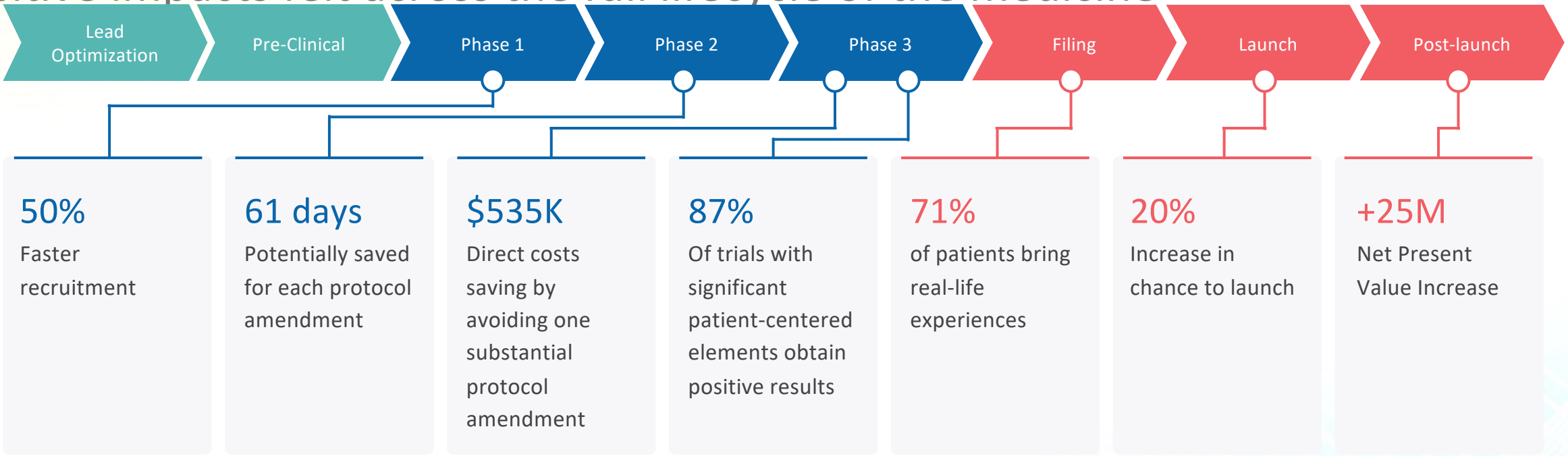
Provided feedback on aspect of study protocols,

Sought advice on which patient support tools should be offered to clinical trial participants (e.g., Welcome Box, Mobile Nursing Visits)

Influenced clinical trial country and site selection

The added value when patient engagement is done right

- Positive impacts felt across the full lifecycle of the medicine



Clinical Outcome Assessments in Clinical Development

Betsy Williams

Polling question 3

My clinical team includes the patient (or caregiver) perspective when considering what COAs to utilize to support clinical trial endpoints?

- Yes – my team involved patients / caregivers and includes their perspective
- Maybe – I am not sure of the process
- No – my team typically selects COAs based on whatever was used previously

Patient reported outcomes (PROs) are one type of Clinical Outcome Assessment

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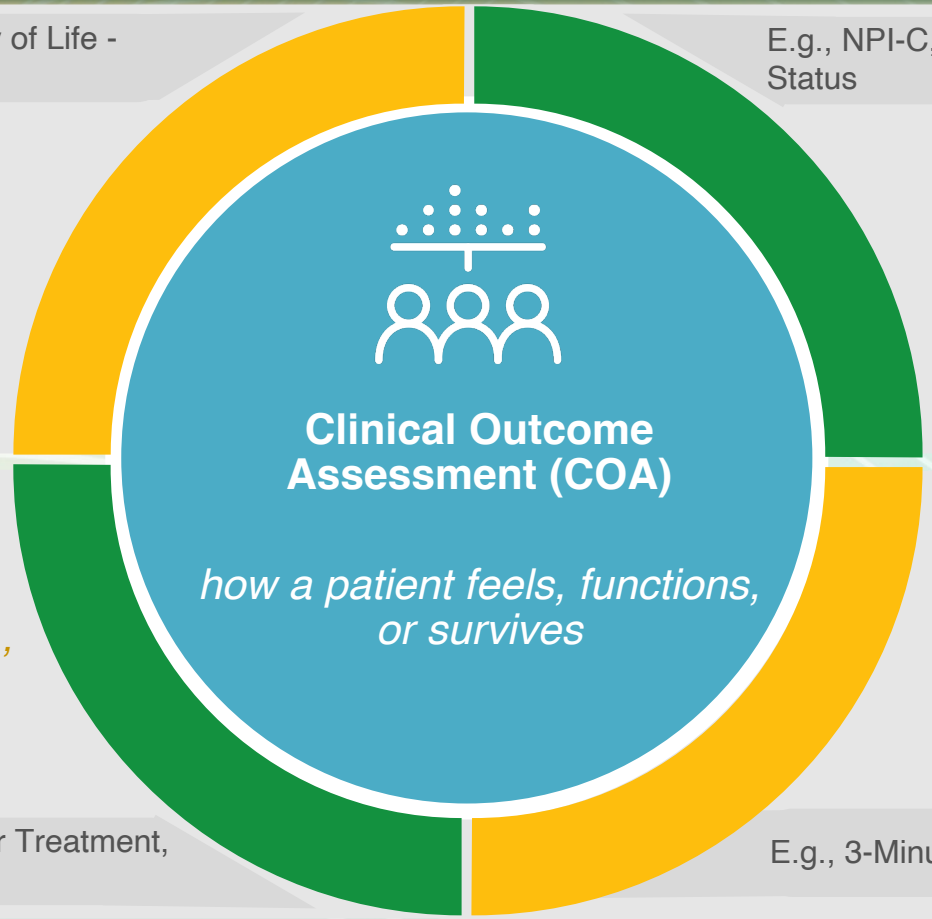

E.g., EORTC EQ-5D-5L, Short-Form 36, Quality of Life - Breast Cancer Scale

Patient-Reported Outcome (PRO)
directly from the patient

E.g., NPI-C, Palliative Prognosis Score, ECOG Performance Status

Clinician-Reported Outcome (ClinRO)
performed by a trained medical professional

Observer-Reported Outcome (ObsRO)
performed by an observer (i.e., a non-clinician, such as a teacher or caregiver)

E.g., Pediatric Functional Assessment of Cancer Treatment, Pediatric Quality of Life Inventory-Parent Report

Performance Outcome (PerfO)
based on a task(s) performed by a patient

E.g., 3-Minute Stair Climb Test, Functional Reach Test

Patient-Focused Drug Development (PFDD) accelerated with the 21st Century Cures Act and led to development of FDA's PFDD guidances

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2020-23

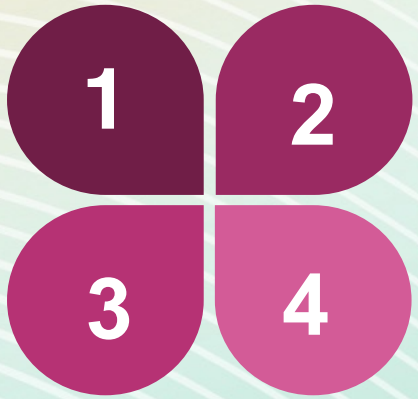
4 Patient-Focused Drug Development Guidances for Industry

Collecting Comprehensive and Representative Input

- Who do you get input from and why?
- How do you collect the information?
- Sampling methods, relationship between research question and methods when deciding from whom to get input
- ***Final Guidance** issued June 2020*

Methods to Identify What is Important to Patients

- What do you ask and why?
- How do you ask non-leading questions that are well-understood by a wide range of patients and others?
- Best practices for qualitative research
- ***Final Guidance** issued Feb 2021*



Selecting, Developing or Modifying Fit-for-Purpose COAs

- How do you decide what to measure in a clinical trial to show clinical benefit?
- How do you select or develop fit-for-purpose clinical outcome assessments?
- **Discussion Document issued Q3 2018**
- ***Draft Guidance** June 2022*

Incorporating COAs into Endpoints for Regulatory Decision Making

- Once you have a COA and a way to collect data using it, what is an appropriate clinical trial endpoint?
- How would you define a meaningful change in that endpoint?
- **Discussion Document issued Q4 2019**
- ***Draft Guidance** April 2023*

EMA's *Regulatory Science Strategy to 2025* report indicates harmonization with FDA

The EMA's 'Regulatory Science Strategy to 2025'

The EMA proposed that the core recommendation is expanded from "*Reinforce patient relevance in evidence generation*" to "***Ensuring the patient voice is systematically incorporated throughout drug development & associated evidence generation***"

5 Strategic Goals for Regulatory Science

- Goal 1: Catalysing the integration of science and technology in medicines development
- Goal 2: Driving collaborative evidence generation improving the scientific quality of evaluations
- **Goal 3: Advancing patient-centered access to medicines in partnership with healthcare systems**
- Goal 4: Addressing emerging health threats and availability/therapeutic challenges
- Goal 5: Enabling and leveraging research and innovation in regulatory science

EMA Regulatory Strategy 2025

Goal 3: Advancing patient-centered access to medicines in partnership with healthcare systems

"Reinforce patient relevance in evidence generation"

- **Revise** the **existing** patient engagement methodology and review and update the EMA's existing **framework for interaction with patients** and patient organisations to reflect EMA's evolving approach to patient data and enhanced patient involvement in EMA scientific committees:
- **Explore** and deploy **additional methodologies** to collect and use patient data for benefit-risk assessment
- **Update** existing, and develop new EMA **guidelines** on patient data collection
- Coordinate the approach to patient reported outcome (PROs)
- **Promote use of core** health-related quality-of life **PROs**

EMA Regulatory Strategy 2025

EMA Regulatory Science to 2025 (europa.eu)

FDA and EMA have identified oncology as an area of opportunity for use of PED

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Mature scientific methods and regulatory frameworks

Increased focus in legislation

Elevated interest in tolerability for novel complex treatment regimens

> PRO measures may provide important patient perspective on the disease and the treatment received; an evaluation that provides **clinically important information** that is **not captured by conventional** anti-tumour **efficacy data and adverse event reporting**
>
> International regulatory agencies have acknowledged that the accurate measurement of the patient experience can complement existing measurements of safety and efficacy in regulatory decision making…sustained international collaboration is underway to advance regulatory science related to PRO measurements

EMA. Reflection Paper on the use of patient-reported outcome (PRO) measures in oncology studies. 2014; EMA/CHMP/292464/2014
Kluetz et al. Focusing on Core Patient-Reported Outcomes in Cancer Clinical Trials: Symptomatic Adverse Events, Physical Function, and Disease-Related Symptoms. Clinical Cancer Research. 2016;22(7):1553-58
Kluetz et al. (2018) Incorporating the patient experience into regulatory decision making in the USA, Europe, and Canada. The Lancet Oncology. VOLUME 19, ISSUE 5, 267-274

FDA's Oncology Review Division has shown willingness to incorporate strong PRO data into product labelling

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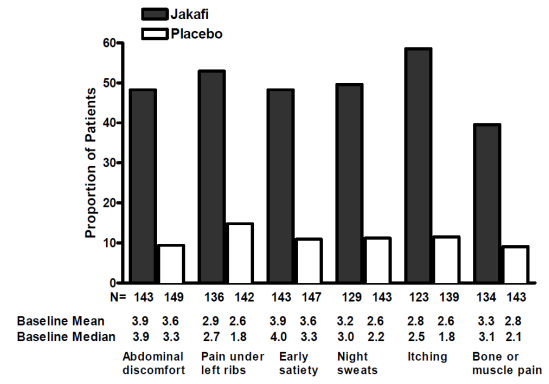
Jakafi® ruxolitinib (tablets)

Figure 3: Proportion of Patients With 50% or Greater Reduction in Individual Symptom Scores at Week 24



ZYKADIA™ ceritinib 150 mg capsules

Exploratory analyses of patient-reported outcome measures suggested a delay in time to development of or worsening of shortness of breath in patients treated with ZYKADIA as compared to chemotherapy. The patient-reported delay in onset or worsening of shortness of breath may be an overestimation, because patients were not blinded to treatment assignment.

RituxanHYCELA™ rituximab/hyaluronidase human subcutaneous injection 1,400 mg/23,400 Units 1,600 mg/26,800 Units

14.4 Patient Experience
Previously untreated adult patients outside of the United States with CD20+ diffuse large B-cell lymphoma (DLBCL) or CD20+ follicular non-Hodgkin's lymphoma (FL) Grades 1, 2, or 3a were randomized to receive a standard chemotherapy regimen (CHOP, CVP, or bendamustine) and either RITUXAN HYCELA 1,400mg/23,400 Units at Cycles 2–4 (after the first cycle with intravenous rituximab) or a rituximab product by intravenous infusion at Cycles 1–4. After the fourth cycle, patients were crossed over to the alternative route of administration for the remaining 4 cycles. After Cycle 8, 477 of 620 patients (77%) reported preferring subcutaneous administration of RITUXAN HYCELA over intravenous rituximab and the most common reason was that administration required less time in the clinic. After Cycle 8, 66 of 620 patients (11%) preferred rituximab intravenous administration and the most common reason was that it felt more comfortable during administration. Forty eight of 620 patients (7.7%) had no preference for the route of administration. Twenty nine subjects of 620 (4.7%) received Cycle 8 but did not complete the preference questionnaire.

Case Study: Consideration of PROs in clinical development

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Situation

- Company X had a product for treatment of male androgenic alopecia (AGA) in development
- Lack of alignment with FDA on Company X's selected COA ("PRO A") supporting Phase 3 endpoints had stalled development
  - PRO A was successfully used by competitor and included in labeling
  - PRO A was developed prior to current FDA COA guidance
- Evidence to support what was important to patients was lacking
- Evidence that PRO A was fit for purpose in Company X's proposed context of use was lacking

Solution

- Concept elicitation interviews were conducted to confirm what symptoms and impacts were important to patients
- Developed an additional PRO ("PRO S") to evaluate the core symptom of AGA and another to evaluate the impacts ("PRO I") of AGA on the lives of patients
- Conducted cognitive debriefing interviews to test PRO A, PRO S, and PRO I with patients
- Based on the data gathered, Company X decided to move forward with PRO S and PRO I
- Developed qualitative report to describe the content validity for newly developed "de novo" PROs

Result

- Developed COA strategy report for FDA alignment on the endpoint strategy and use of de novo PROs in Phase 3
- Psychometric evaluation of de novo PROs planned as next steps
- First-in-disease PRO evaluating impacts of AGA

Potential consequences of *not* including COAs in clinical trials

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Insufficient study design

- Not understanding patient's most pressing needs with a disease can **reduce ability to recruit** (meaningfulness of trial for patients despite survival) **and retain** (trial procedures, expectations) patients for trials
- Risk to **prioritizing endpoints appropriately**
- Potential **regulatory** request to add measure for assessing impact of treatment on patient experience
- Not fit-for-purpose COA measures or insufficient assessment schedules that **unnecessarily increases patient burden**

Regulatory consequences can lead to significant additional costs

"For a pre–phase 2 project, the cumulative impact of a patient engagement activity that avoids one protocol amendment and improves enrollment, adherence, and retention is an **increase in net present value (NPV) of $62MM ($65MM for pre–phase 3) and an increase in ENPV of $35MM ($75MM for pre–phase 3)**. Compared with an investment of $100,000 in patient engagement, the **NPV and ENPV increases can exceed 500-fold** the investment".

Fail to convince patients and HCPs

- **Low perceptions of credibility and applicability** of findings; patients and HCPs as increasingly looking for patient experience data to contextualize results
- Lower quality of **knowledge translation materials**
- Lower likelihood for involvement in **clinical guidelines**

Disadvantages for companies in terms of relationship building and adopting FDA's mission

FDA increasingly recommends and advocates for patient-focused drug development; companies disregarding FDA recommendations may harm relationship

Market access and launch complications

- Payers, specifically Germany and France, are more likely to give **"preferential pricing" to assets with COA data**
- Without COAs, **missed opportunity for product differentiation** to similar compounds, particularly in big disease
- **Competitive products** can **experience advantage** if they provide COA data to support their claims as they market their products

Levitan B, Getz K, Eisenstein EL, Goldberg M, Harker M, Hesterlee S, Patrick-Lake B, Roberts JN, DiMasi J. Assessing the Financial Value of Patient Engagement: A Quantitative Approach from CTTI's Patient Groups and Clinical Trials Project. Ther Innov Regul Sci. 2018 Mar;52(2):220-229. doi: 10.1177/2168479017716715. Epub 2017 Jul 17. PMID: 29714515; PMCID: PMC5933599.
Reaney M. et all, "Using Patient Experience Data to Evaluate Medical Interventions", 2023

Questions

Thank you!

Appendix/Additional Slides

Patient-Focused Drug Development (PFDD) accelerated with the 21st Century Cures Act

2016

21st Century Cures Act

- Law **includes an initial definition** of the term patient experience data: **"Patient experience data can be interpreted as information that captures patients' experiences, perspectives, needs, and priorities** related (but not limited to):
  1. Symptoms of their condition and natural history
  2. Impact of the conditions on functioning and quality of life
  3. Experiences with treatment
  4. Input from patients on which outcomes are important to them
  5. Patient preferences for outcomes and treatments
  6. The relative importance of any issue as defined by patients"

FDA acknowledges the importance of:

- ✓Generating reliable and valid data
- ✓Ensuring interpretable outcomes
- ✓Comprehensively understanding both benefits (efficacy) and risks/harms (safety) to inform decision-making

The EMA's 'Regulatory Science Strategy to 2025' is aligned: "Ensuring the patient voice is systematically incorporated throughout drug development & associated evidence generation"

- **Mandates the US FDA to develop guidance** on collection and use of PED and related information in drug development

21 USC 360bbb–8c note.

SEC. 3002. PATIENT-FOCUSED DRUG DEVELOPMENT GUIDANCE.

(a) PUBLICATION OF GUIDANCE DOCUMENTS.—Not later than 180 days after the date of enactment of this Act, the Secretary of Health and Human Services (referred to in this section as the "Secretary"), acting through the Commissioner of Food and Drugs, shall develop a plan to issue draft and final versions of one or more guidance documents, over a period of 5 years, regarding the collection of patient experience data, and the use of such data and related information in drug development. Not later than 18 months after the date of enactment of this Act, the Secretary shall issue a draft version of at least one such guidance document. Not later than 18 months after the public comment period on the draft guidance ends, the Secretary shall issue a revised draft guidance or final guidance.

PUBLIC LAW 114–255—DEC. 13, 2016 130

(b) PATIENT EXPERIENCE DATA.—For purposes of this section, the term "patient experience data" has the meaning given such term in section 569C of the Federal Food, Drug, and Cosmetic Act (as added by section 3001).

(c) CONTENTS.—The guidance documents described in subsection (a) shall address—

(1) methodological approaches that a person seeking to collect patient experience data for submission to, and proposed use by, the Secretary in regulatory decisionmaking may use, that are relevant and objective and ensure that such data are accurate and representative of the intended population, including methods to collect meaningful patient input throughout the drug development process and methodological considerations for data collection, reporting, management, and analysis;

odological approaches that may be used to develop what is most important to patients with respect f disease, burden of treatment, and the benefits the management of the patient's disease;

oaches to identifying and developing methods to acts to patients that will help facilitate collection perience data in clinical trials;

hodologies, standards, and technologies to collect clinical outcome assessments for purposes of regu- nmaking;

a person seeking to develop and submit proposed ce relating to patient experience data for consider- Secretary may submit such proposed draft guidance ary;

ormat and content required for submissions under to the Secretary, including with respect to the described in paragraph (1);

the Secretary intends to respond to submissions ion described in paragraph (1), if applicable, y timeframe for response when such submission of a regulatory application or other submission associated timeframe for response; and

the Secretary, if appropriate, anticipates using tient experience data and related information, including with respect to the structured risk-benefit assessment framework described in section 505(d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(d)), to inform regulatory decisionmaking.

https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf

Section 3001 of Cures Act requires FDA to publicly report PED considered in approval of drug application

The Patient Experience Data Table provides a mechanism for reviewers to summarize the types of patient experience data that the applicant submitted as part of their application, whether they discussed the data in their review of the application, and whether they considered patient experience data from other sources

Patient Experience Data Relevant to this Application (check all that apply)

				Section of review where discussed, if applicable
1	☐	The patient experience data that were submitted as part of the application include:		
2		☐	Clinical outcome assessment (COA) data, such as	
3			☐ Patient reported outcome (PRO)	
4			☐ Observer reported outcome (ObsRO)	
5			☐ Clinician reported outcome (ClinRO)	
6			☐ Performance outcome (PerfO)	
7		☐	Qualitative studies (e.g., individual patient/caregiver interviews, focus group interviews, expert interviews, Delphi Panel, etc.)	
8		☐	Patient-focused drug development or other stakeholder meeting summary reports	
9		☐	Observational survey studies designed to capture patient experience data	
10		☐	Natural history studies	
11		☐	Patient preference studies (e.g., submitted studies or scientific publications)	
12		☐	Other: (Please specify):	
13	☐	Patient experience data that were not submitted in the application, but were considered in this review:		
14		☐	Input informed from participation in meetings with patient stakeholders	
15		☐	Patient-focused drug development or other stakeholder meeting summary reports	
16		☐	Observational survey studies designed to capture patient experience data	
17		☐	Other: (Please specify):	
18	☐	Patient experience data was not submitted as part of this application.		

Source DOI: 10.1177/2168479019871519. ; https://www.fda.gov/media/150405/download

June 2021 report published by FDA assessed use of PED in regulatory decision-making

- Of NME NDAs and BLAs in the assessment cohort, **68%** of FDA reviews mention patient experience data
- 82% of these reviews include a Patient Experience Data Table

Metric		FDA Reviews of Approved NME NDAs and BLAs (n=176)		
		All (n=176)	Priority Review (n=112)	Orphan (n=87)
Percent of approved applications where review documents mention patient experience data		68%	70%	66%
	Percent of approved applications where review documents mention patient experience data from **the application****	66%	66%	62%
	Percent of approved applications where review documents mention patient experience data from **other sources****	7%	9%	11%

*NME NDAs and BLAs received by FDA between June 12, 2017 and June 12, 2020, and approved by CDER or CBER by February 5, 2021.

**Percentages sum to more than 68% (all NME NDAs/BLAs), 70% (Priority Reviews) or 66% (Orphan designation) because some review documents mention patient experience data from both the application and other sources.

https://www.fda.gov/media/150405/download

PROs are the main types of PED mentioned by FDA in their reviews; however, many types of PED can be considered

Table 2-5. Results of metrics for patient experience data in approved product labeling*

Metric	Product Labeling for Approved NME NDAs and BLAs with FDA Reviews that mention Patient Experience Data (n=36)
Percent of approved product labeling that mentions patient experience data	30%
Special Feature	
Percent of approved product labeling with patient experience data for applications with special feature: **Priority Review****	53%
Percent of approved product labeling with patient experience data for applications with special feature: **None****	44%
Percent of approved product labeling with patient experience data for applications with special feature: **Orphan****	39%

The report found that found that 30% of approved product labeling for NME NDAs and BLAs mentioned PED

PROs and other COAs are the types of PED most likely to serve as endpoints in clinical trials (and are therefore mostly likely to be considered in risk-benefit analyses and approval decisions)

Metric	FDA Reviews that Contain PED for Approved NME NDAs and BLAs (n=120)
Of FDA reviews that mention patient experience data, percent that mention data from **applicants**	97%
• PRO	84%
• ClinRO	33%
• PerfO	9%
• ObsRO	7%
• Patient preference study	3%
Of FDA reviews that mention patient experience data, percent that mention data from **other sources**	11%
• PFDD meetings	4%
• Natural history study	3%

PED = Patient Experience Data. PRO = Patient-Reported Outcome. ClinRO = Clinician-Reported Outcome. PerfO = Performance Outcome. ObsRO = Observer-Reported Outcome.

*NME NDAs and BLAs received by FDA between June 12, 2017 and June 12, 2020, and approved by CDER or CBER by February 5, 2021.

**Percentages sum to more than 100% because some review documents mention patient experience data from both the application and other sources.

https://www.fda.gov/media/150405/download

EMA pilot project led to commitment from CHMP to involve patients in oral explanations where they see benefit

Bringing the patient perspective to the work of the Agency

2014-2016: EMA conducted a pilot project to involve patients directly in the assessment of the benefits and risks of 6 medicines in its CHMP. Since then, it has been decided that the **CHMP will continue to involve patients in CHMP oral explanations** when it is felt this could be of benefit

In addition, patient representatives are already involved in many other activities, e.g., in the capacity of:

- **Full members of EMA committees;** the Pharmacovigilance Risk Assessment Committee, the Paediatric Committee, the Committee for Advanced Therapies and the Committee for Orphan Medicinal Products
- **Experts** within **scientific advice** procedures
- **Experts** in the various scientific advisory groups (SAGs), which provide specialized advice to the Agency's scientific committees on the **benefit-risk evaluation** of specific types of medicines or treatments
- **Experts** reviewing **documents for the public** prior to publication, such as package leaflets, EPAR summaries, herbal summaries and safety communications
- **Members** of the **Patients' and Consumers' Working Party**, through which they provide recommendations to the Agency and its human scientific committees on all matters of interest to patients in relation to medicines

https://www.ema.europa.eu/en/documents/report/outcome-report-pilot-involve-patients-benefit/risk-discussions-chmp-meetings_en.pdf

Oncology-focused guidance on COAs was released in 2021 by FDA's Oncology Center of Excellence

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KEY Points

1. **Includes recommendations for a core set of PRO measures for use in cancer clinical trials**
2. **Outlines considerations for instrument selection and trial design**

Scope

- Specific to registration trials for **anti-cancer** therapies intended to **demonstrate an effect on survival, tumor response, or delay in the progression of a malignancy**
- Improvements in patient-reported symptoms or functional impacts alone is outside the scope of the guidance

Agencies' recommendation

- **A core set of PRO measures** to maximize the utility of submitted PRO information

  More details under agenda point "Principles in designing Clinical Outcome Assessments and Patient-Centered Endpoints"

- **Assessment frequency (trial design)**

  The recommendation is very determined and should be taken with a grain of salt. However, it becomes clear that FDA wants to see more and earlier PRO data (particularly for the first 6 months)

Figure 1: Example PRO assessment frequency for first 12 months of advanced cancer trial

	Standard 6 month treatment period												Follow-up		
	BL	w 2	w 3	w 4	w 5	w 6	w 7	w 8	M 3	M 4	M 5	M 6	M 9	M12	*
Symptomatic AE[16]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Single Item Side Effect Global	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Physical Function	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Role Function	X		X		X		X		X	X	X	X	X	X	
Disease Symptoms	X				X				X			X		X	
Other HRQOL	X								X			X		X	

BL – baseline, w - week, M - month, * - context dependent long-term follow-up

Source: FDA Draft Guidance for Industry Core Patient-Reported Outcomes in Cancer Clinical Trials, June 2021 Draft Guidance: Core Patient-Reported Outcomes in Cancer Clinical Trials (fda.gov)