Innovative approaches to collecting more precise patient experience data for oncology clinical trials

Kelly Dumais, PhD
Director, eCOA Science and Consulting

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Agenda

1. History and evolution of patient-reported outcome (PRO) data collection in oncology trials, including the regulatory landscape
2. Best practices and innovative methods for collecting what matters to the patient
3. Operational considerations for enhanced patient experience

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History and evolution of Oncology PROs

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Use of COAs in Oncology trials is less than in non-oncology trials

"18% of oncology trials reported COA use as determined by the search for individual instruments among trial design entries related to outcomes."

vs. 26% of non-oncology trials

TABLE 1 Rate of clinical outcomes assessment (COA) use and associations with trial characteristics via logistic regression.

	COA use			
	Oncology ($N = 7339$ reporting all data)		Non-oncology ($N = 31,481$ reporting all data)	
Trial characteristics	% using COAs (n)	OR (p)	% using COAs (n)	OR (p)
Phase (ordinal)	$N = 26,828$[a]	**1.30 (<0.001)**	$N = 132,379$	**1.17 (<0.001)**
Early phase 1	11.71% (65/555)	–	19.38% (534/2756)	–
Phase 1	6.89% (331/4806)	–	8.71% (2504/28,749)	–
Phase 1/phase 2	10.87% (314/2889)	–	20.93% (1749/8355)	–
Phase 2	14.81% (1888/12,745)	–	26.02% (8708/33,461)	–
Phase 2/phase 3	24.83% (144/580)	–	28.11% (1390/4944)	–
Phase 3	30.4% (1325/4358)	–	30.22% (8373/27,711)	–
Phase 4	19.22% (172/895)	–	23.98% (6331/26,403)	–

An analysis of 279,855 interventional trials with start dates between 1985 and 2020 from clinicaltrials.gov

Kim et al Cancer Medicine, 2023;00:1-13 https://onlinelibrary.wiley.com/doi/epdf/10.1002/cam4.6325

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Growing interest in oncology PROs

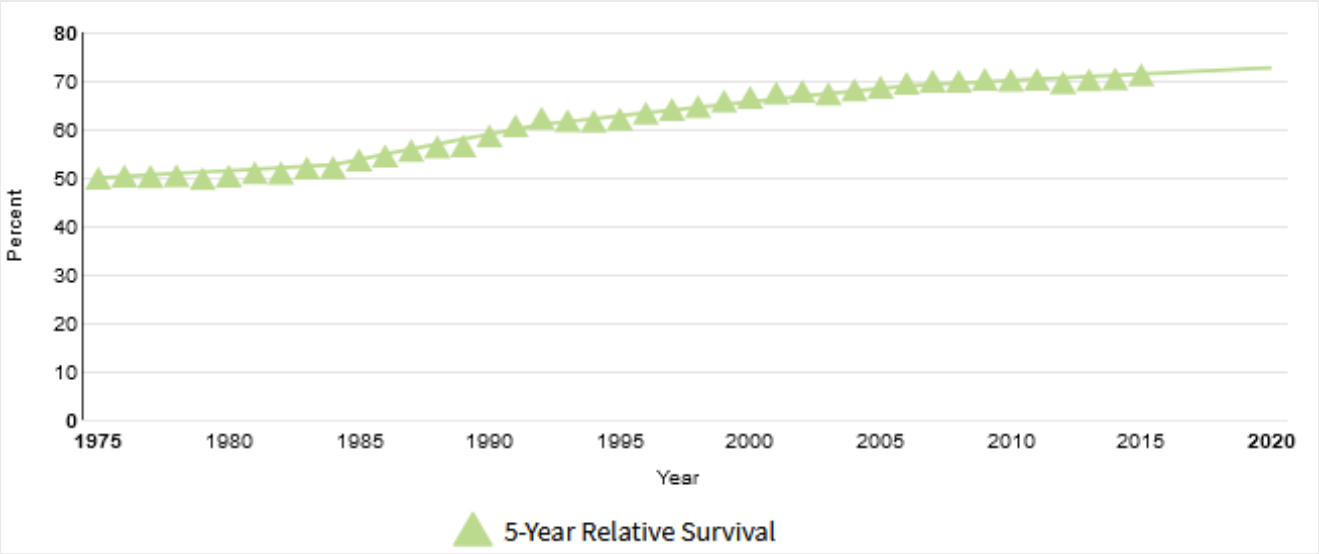
Focus on the patient

Patients ***should*** and ***want*** to know how they will feel on treatment

Survival rates are increasing[1]

- In 2020, there were an estimated **17,113,494 people** living with cancer in the United States

It's not just about survival, but how patients are living with cancer



[1] NIH, National Cancer Institute, https://seer.cancer.gov/statfacts/html/all.html

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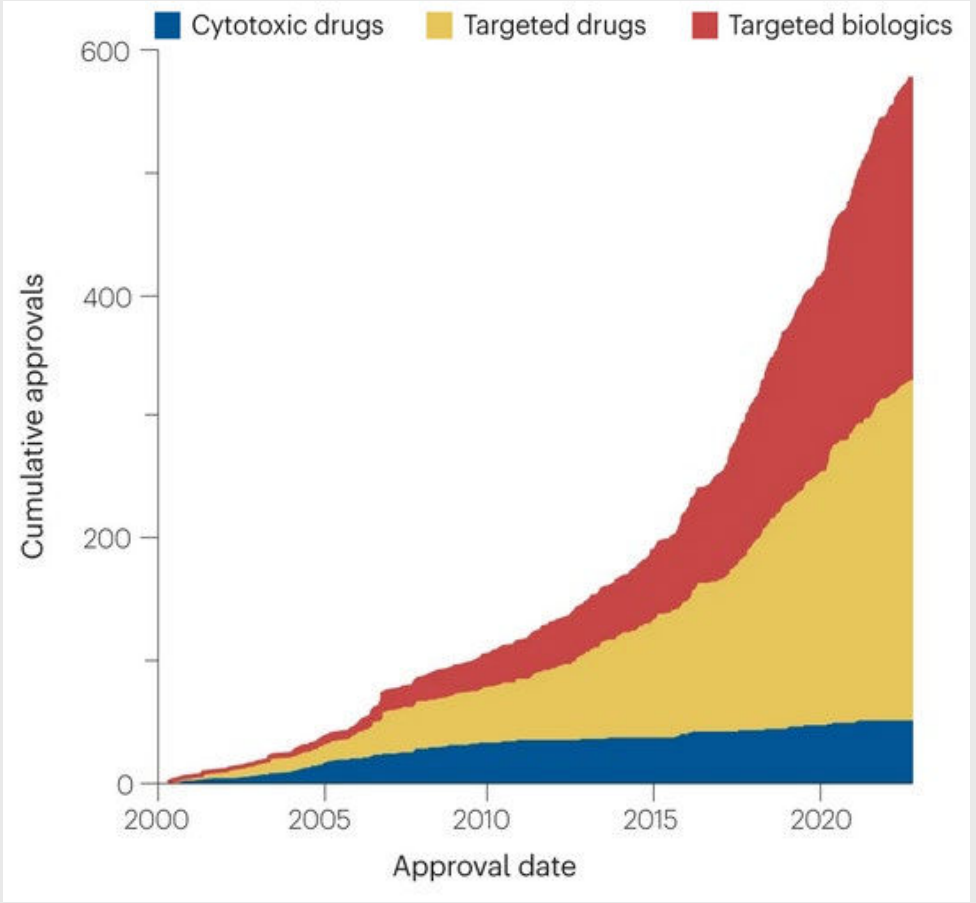
Growing interest in oncology PROs

Competitive market landscape

There were **573 oncology indication approvals** granted for 206 distinct oncology products between Jan 2000 – Oct 2022 [2]

Increasing rate of oncology drug approvals over time

- Mean annual approvals increased **from 7.4 per year** for 2000–2004 to **56 per year** for 2017–2022 (a 757% increase)[2]



[2] Scott et al Nature Reviews Drug Discovery; 2023:22:625-640

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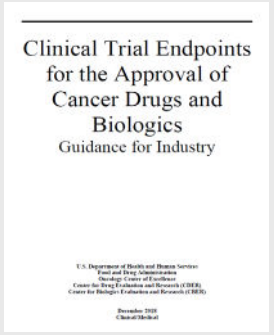
Growing interest in oncology PROs

Regulatory landscape

FDA's 1st Annual Workshop on COAs in Cancer Clinical Trials

2016

FDA Oncology Guidance Update

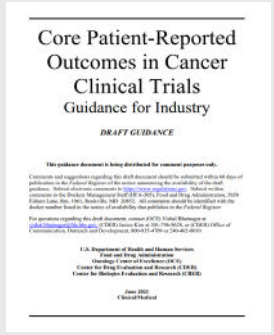

Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics
Guidance for Industry

Dec 2018

FDA launches Project Patient Voice

June 2020

FDA Core PROs in Oncology, draft


Core Patient-Reported Outcomes in Cancer Clinical Trials
Guidance for Industry
DRAFT GUIDANCE

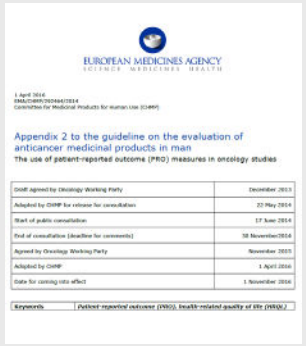
June 2021

FDA's 8th Annual Workshop on COAs in Cancer Clinical Trials

27 June 2023

April 2016

EMA Appen. 2 PROs in Oncology


EUROPEAN MEDICINES AGENCY
Appendix 2 to the guideline on the evaluation of anticancer medicinal products in man
The use of patient-reported outcome (PRO) measures in oncology studies

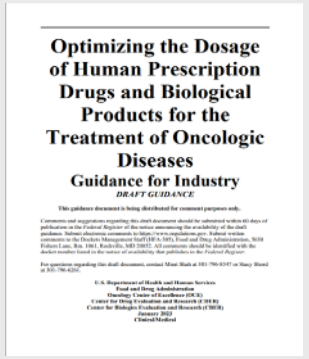
Oct 2020

EMA Oncology Guidance Update


EUROPEAN MEDICINES AGENCY
Guideline on the clinical evaluation of anticancer medicinal products

Jan 2023

FDA Dose Optimization, draft


Optimizing the Dosage of Human Prescription Drugs and Biological Products for the Treatment of Oncologic Diseases
Guidance for Industry
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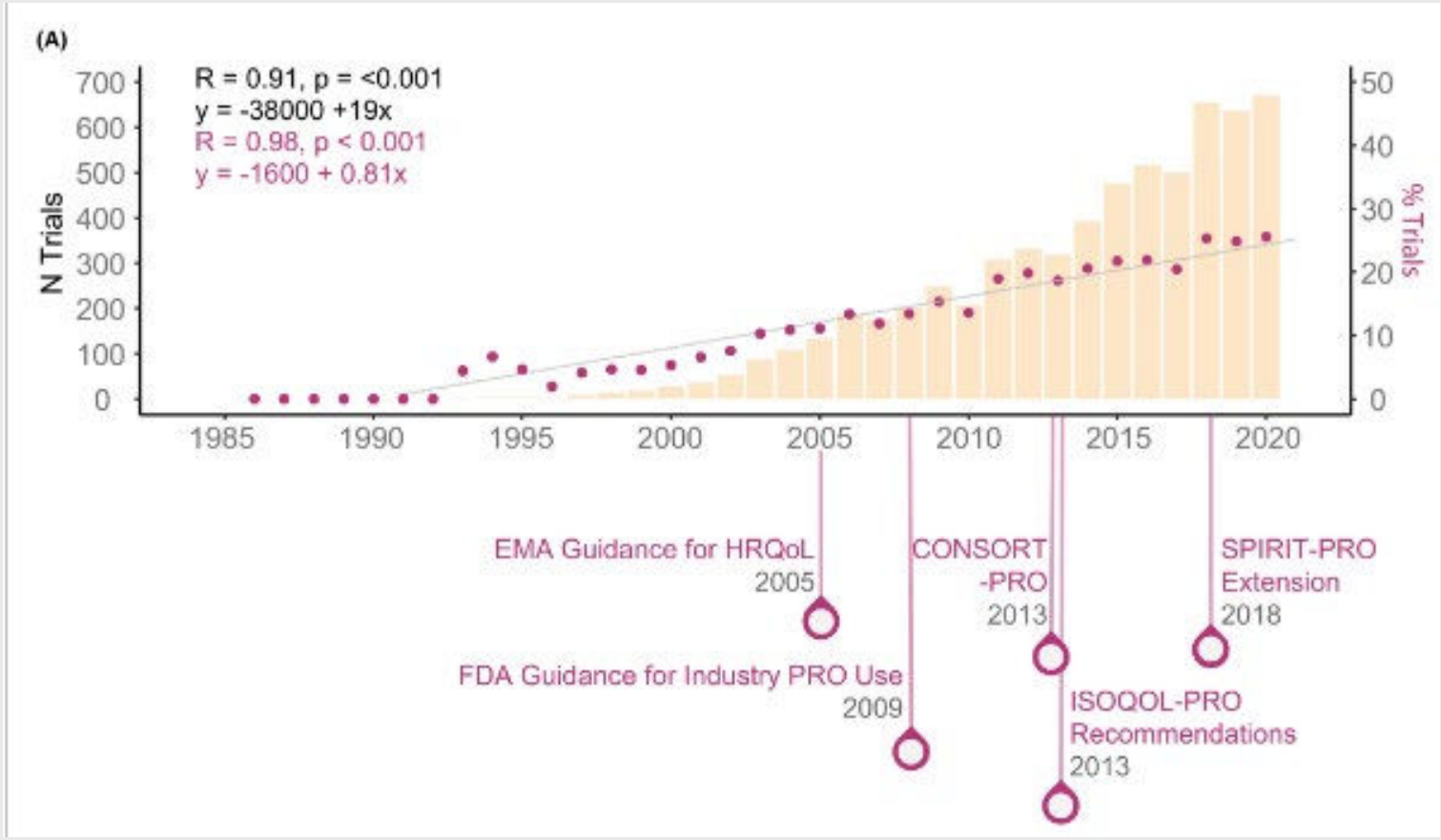
Oncology clinical trials using COAs over time

New regulatory guidance fuels higher usage of COAs

Both the number and proportion of oncology trials using COAs **increased significantly over time**, at rates of an additional 19 trials per year

Significant increase in COA use **after the five release dates** of regulatory guidelines and interest group recommendations for PROs



Interventional trials with start dates between 1985 and 2020 from clinicaltrials.gov

Kim et al Cancer Medicine, 2023;00:1-13 https://onlinelibrary.wiley.com/doi/epdf/10.1002/cam4.6325

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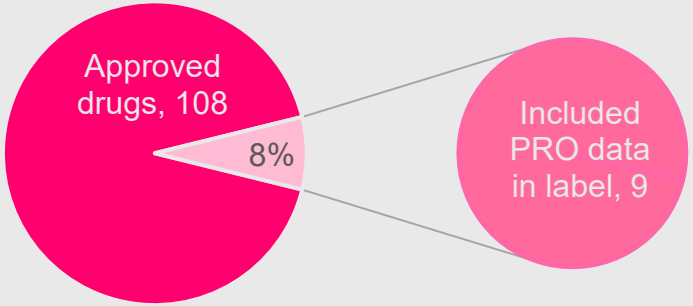
How PRO data is used – for labelling and for informed treatment choice

Labeling from 2010 – 2020

FDA



PRO concepts on label:

- Symptoms (67%)
- Patient preference (33%)

44% were open-label studies

All approved from 2014 onwards

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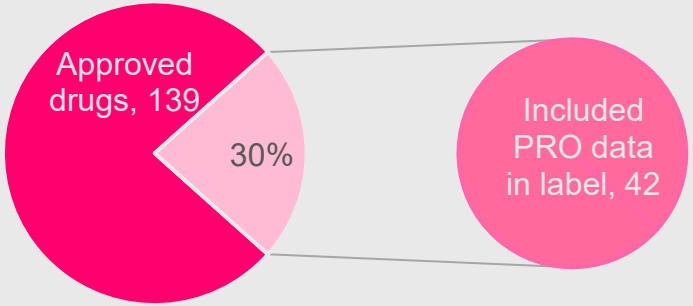


PRO concepts on label:

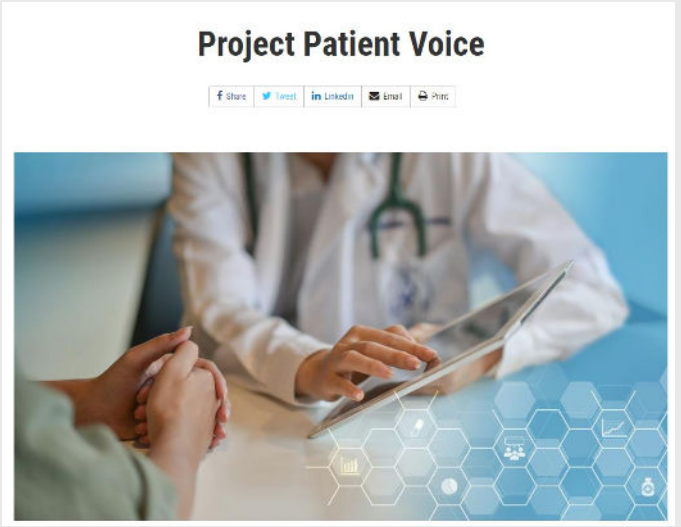
- Health-related QoL (74%)
- Symptoms (32%)
- Functioning (21%)
- Health utility (21%)

49% were open-label studies

77% approved from 2015 onwards

FDA's Project Patient Voice

Publicly available patient experience data to help patients and healthcare providers when talking about the risks and benefits of a drug



Cella et al., 2022 Front Pharmacol; 13: 1031992. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9634749/#s10

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Exploring best practices and collecting what matters to the patient

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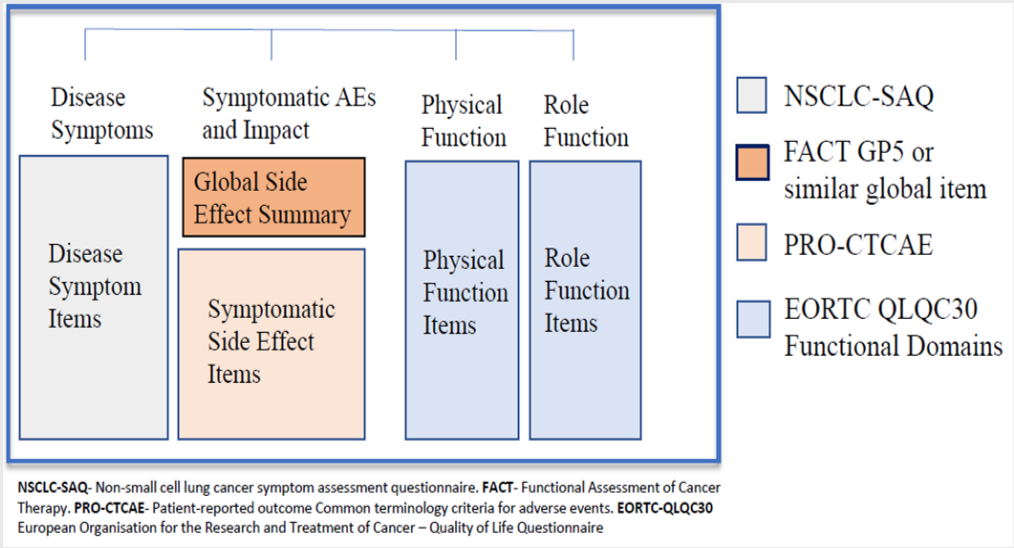
FDA Draft Guidance: Core PROs in cancer clinical trials – June 2021

Core PROs

- Disease-related symptoms
- Physical function
- Role function
- Symptomatic adverse events
- Overall side effect impact summary measure



NSCLC-SAQ- Non-small cell lung cancer symptom assessment questionnaire. **FACT**- Functional Assessment of Cancer Therapy. **PRO-CTCAE**- Patient-reported outcome Common terminology criteria for adverse events. **EORTC-QLQC30** European Organisation for the Research and Treatment of Cancer – Quality of Life Questionnaire

Frequency considerations

- Baseline data, higher frequency in early cycles, consider drug type/schedule

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

PRO assessment:
"last 7 days" recall

PRO assessment:
"last 7 days" recall

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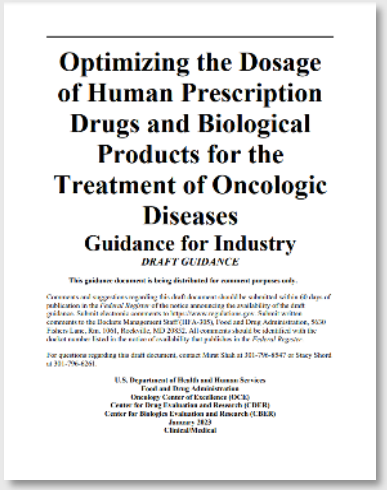
Patient-reported vs. clinician-reported tolerability in oncology



Optimizing the Dosage of Human Prescription Drugs and Biological Products for the Treatment of Oncologic Diseases

Guidance for Industry

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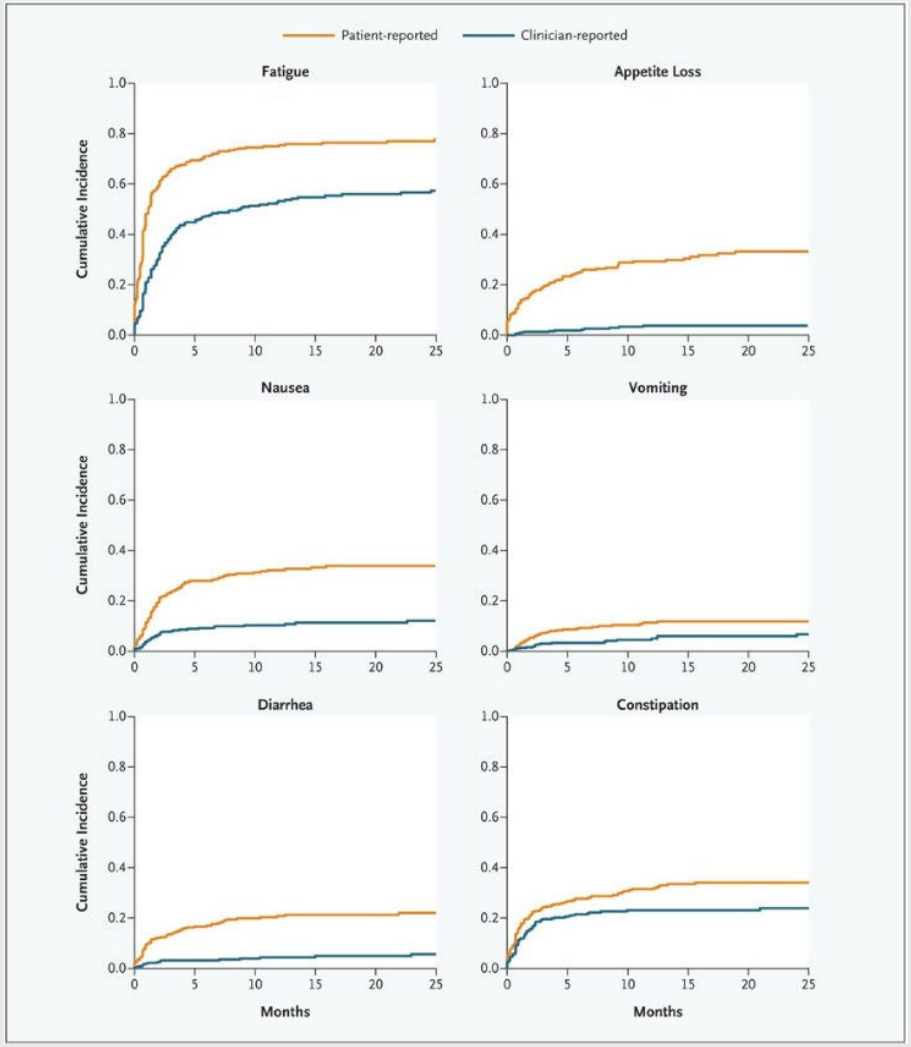
This guidance document is being distributed for comment purposes only.

U.S. Department of Health and Human Services
Food and Drug Administration
Oncology Center of Excellence (OCE)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
January 2023
Clinical/Medical

*"Inclusion of PROs should be considered **to enhance the assessment of tolerability** in early phase dosage finding trials."*



Current practice for collecting AEs assumes that clinicians have an accurate picture of patient's subjective experiences. Yet, clinicians downgrade and miss symptoms

Patients report symptoms earlier and more frequently than do clinicians

Basch E. New England Journal of Medicine. 2010;362(10):865-9. Symptoms measured using NCI-CTCAE system. Health status measured using EQ-5D.

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Modular approach to collecting PROs

Traditional approach: Potential for repetitive PRO concepts

EORTC-QLQ-C30	EORTC QLQ-HL27
5 physical functioning	muscle weakness
2 role function	2 pain
4 emotional function	taste
2 cognitive function	vulnerable veins
2 social function	itching
2 QOL	dyspnea
3 fatigue	3 fatigue
nausea	mood changes
vomiting	confidence
anorexia	restless
dyspnea	body dissatisfaction
diarrhea	self confidence
constipation	accepting limitations
2 pain	10 worried
insomnia	role function
financial	

Modular approach: Removes repetitive questions, ability to add missing items

Functional scales, e.g.:

- Physical function
- Role function
- Emotional function
- Cognitive function
- Social function

+

Individual items, e.g.:

- EORTC Item Library
- MD Anderson Symptom Library
- PRO-CTCAE

2021 Draft FDA Core PROs in Oncology Guidance:

"When using a modular approach where these elements are able to be assessed and analyzed separately, different assessment frequencies can be selected that can reduce the response burden to patients."

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Computerized Adaptive Testing (CAT) approach to collecting PROs

Traditional approach: Potential for irrelevant items, floor and ceiling effects

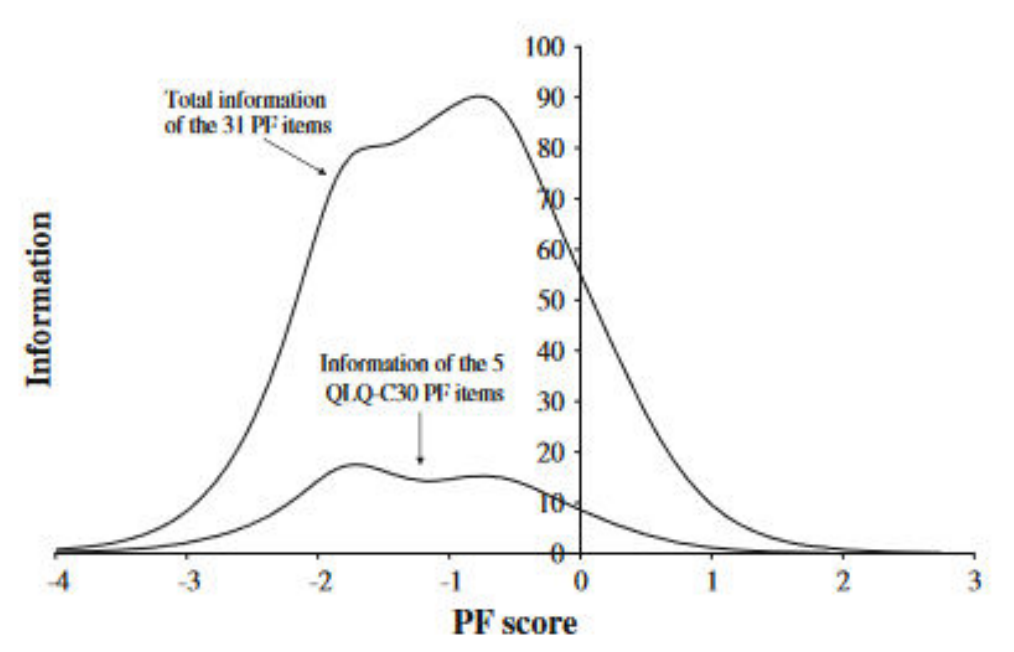

Fig. 1 Test information function for the 31 items in the final model and for the five EORTC QLQ-C30 PF items, respectively

CAT approach: Increases relevance, enhances measurement precision (e.g., EORTC CAT Core)

Items presented to the patient is adapted to the HRQOL level of the individual patient

- if a patient has reported few problems, the next item will ask about a more demanding task
- if a patient reported severe problems, the next item will ask about a less demanding task

Petersen et al, Quality of Life Research, 2011;20(4),479-490

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Wearables and connected devices

Collect objective, high-quality data directly from participants, while minimizing burden

Common outcomes measured:

- Physical activity
- Sleep
- Functional mobility (gait, sway, balance)

Keys for success:

- Scientific validation
- Suitability with patient population
- Simple and intuitive
- Unified patient experience

Clario has devices that measure outcomes in real-time, complemented by guidance on movement-specific protocol development and digital mobility endpoint selection and evaluation

Gait & Posture 69 (2019) 136–142

Contents lists available at ScienceDirect

Gait & Posture

journal homepage: www.elsevier.com/locate/gaitpost

Full length article

Postural sway, falls, and self-reported neuropathy in aging female cancer survivors

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ARTICLE INFO

Keywords:
Postural stability
Balance
Chemotherapy
Mediolateral

ABSTRACT

Background: Falls are a major public health concern in older adults, and the proportion of older adults that has been diagnosed with cancer is growing. Yet, while falls, peripheral neuropathy, and postural instability are more common in aging cancer survivors, it is unclear how these factors interact.
Research question: Our objective was to examine how components of sway related to self-reported neuropathy and falls.
Methods: Postural sway during static stance was recorded with an inertial sensor (APDM Opal), placed on the lumbar spine region in 434 older female cancer survivors (mean age 63) and 40 healthy older female control subjects (mean age 63). Measures of sway were resolved into principal components that were compared between women with and women without self-reported falls in the previous 6 months and between those with and without self-reported symptoms of peripheral neuropathy.
Results: Cancer survivors had worse sway than healthy control subjects in components related to sway magnitude and mediolateral frequency of sway, but no difference in the component related to resultant / AP sway jerk and frequency. Cancer survivors who reported neuropathy were more likely to have higher resultant / AP sway frequencies and jerk than asymptomatic survivors, while survivors who reported a fall were more likely to have lower frequencies of mediolateral sway than non-fallers. Falls were more strongly associated with mediolateral sway in survivors with more severe neuropathy; whereas falls were more strongly associated with resultant / AP sway frequency in survivors with less severe neuropathy
Significance: Postural stability, falls, and neuropathy have complex interactions that can vary across components of postural sway. While the frequency of mediolateral sway was associated with falls across our entire cohort, neuropathy influenced the associations between specific characteristics of sway and falls, which may have implications for fall prevention interventions.

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Operational considerations for patient burden and experience

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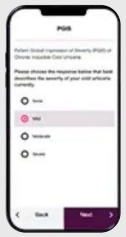
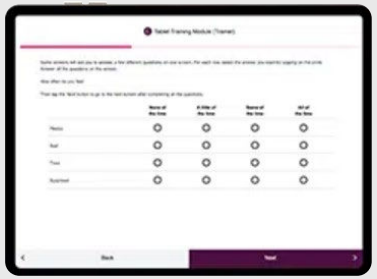
Modality options when using electronic data collection

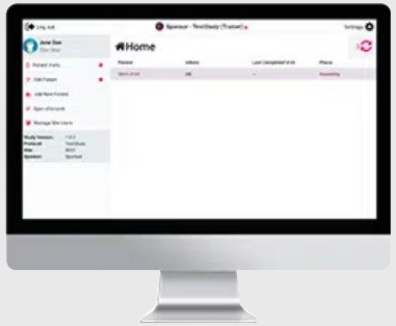


Provisioned devices



Tablets

BYOD



Home computer

Make it easy & convenient for patients so the trial fits into their lives

- What modalities would suit their needs/disease/lifestyle?
- Where to take part – at site, remotely e.g., at home
- Flexibility - devices can be used in different locations/situation

When does each modality work well?

Clario's science team can recommend the right assessments, methods & devices to capture COA depending on your TA, patient population, geographical considerations etc.

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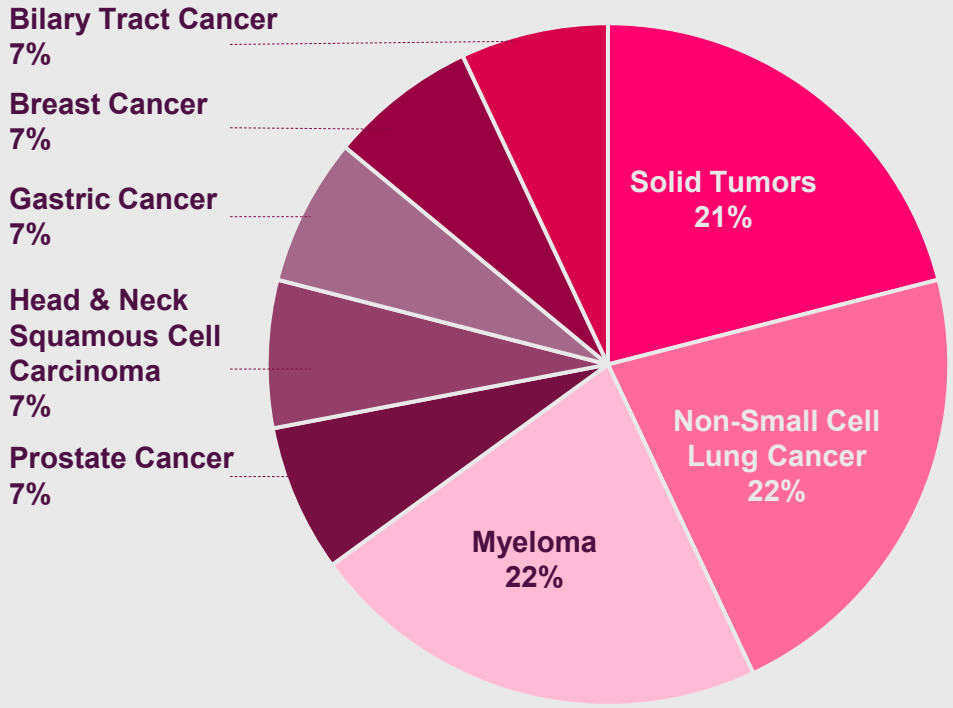
Completion rates and trends of the PRO version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE®) across 14 oncology clinical trials

Clario eCOA Science findings

Feasibility of collecting the electronic PRO-CTCAE®

- How long does it take patients to complete?
- What is the compliance rate?
- Do the number of questions impact compliance?
- Does the length of the study impact compliance?



Distribution of oncology indications

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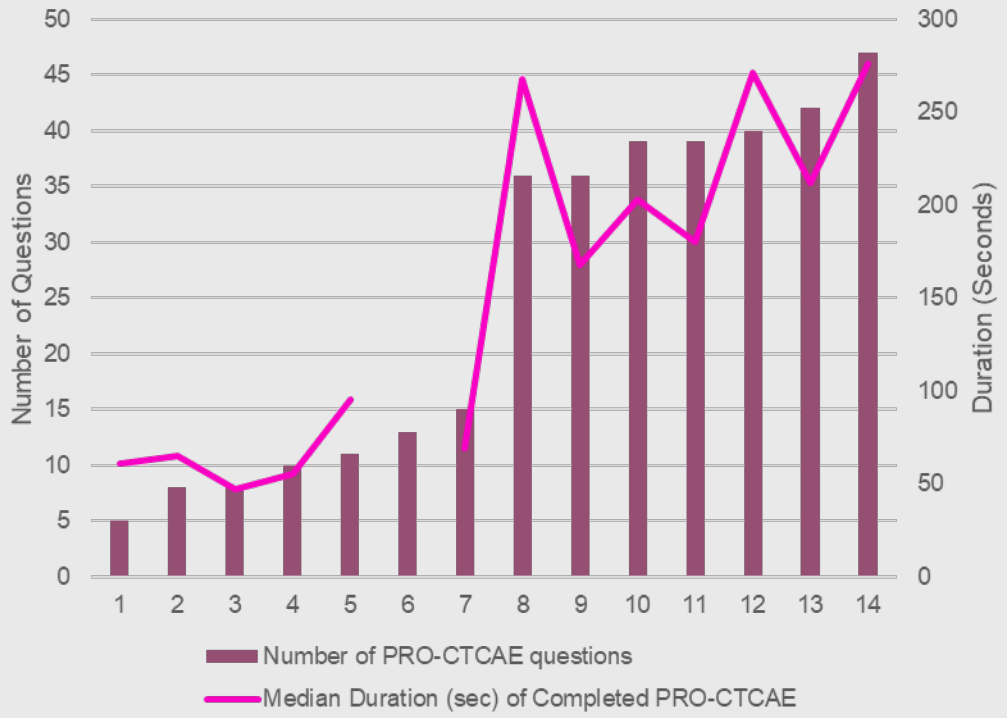
Median time to complete the PRO-CTCAE® across studies is less than 5 minutes

Clario eCOA Science findings



Average number of questions = 25 (range 5-47)
Average number of symptoms = 13 (range 4-25)

Positive association between number of questions and time to complete ($F(1,12) = 78.1$, $p<.001$, $R2$ of .88).

Overall median time to complete PRO-CTCAE = 82s.

Each additional question added 5.2s.

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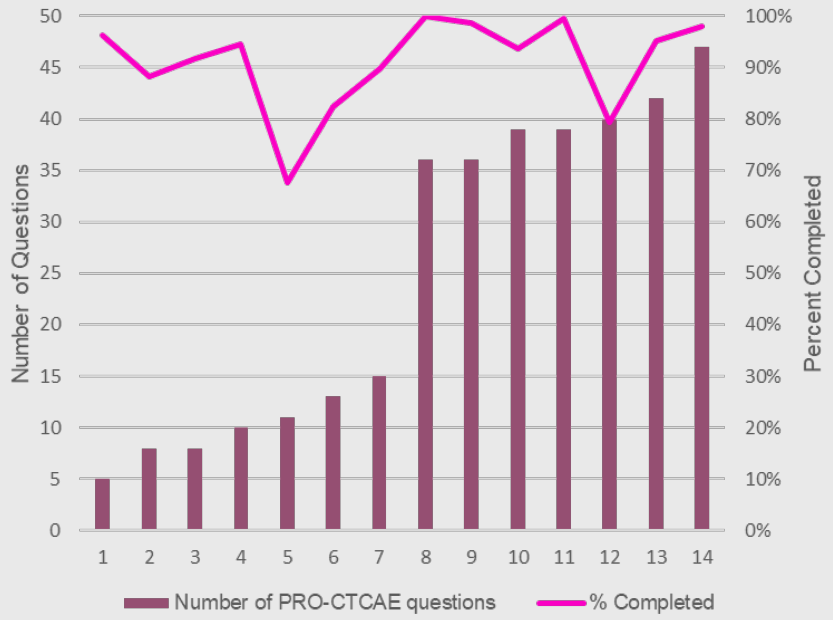
High PRO-CTCAE® compliance across studies, regardless of question # and study duration

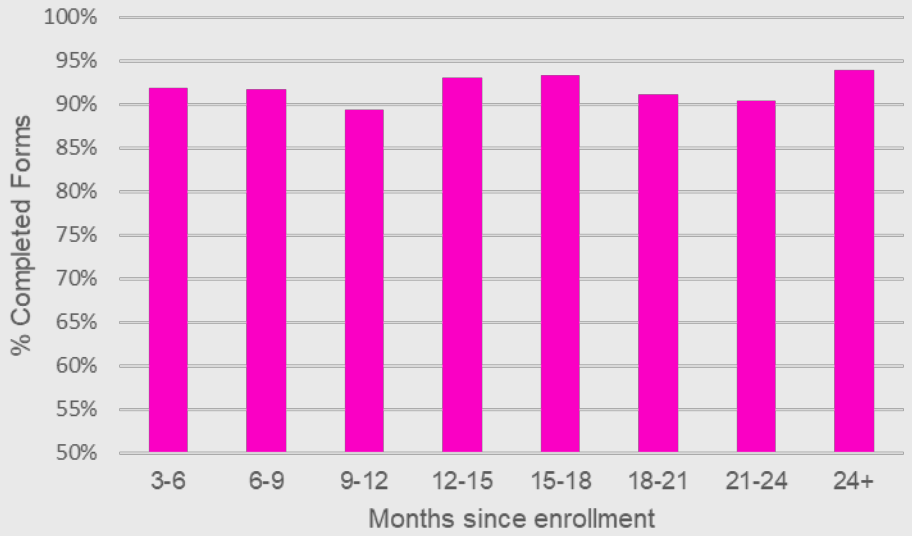
Clario eCOA Science findings

Completion rate was not associated with the number of PRO-CTCAE questions included.

Overall compliance across studies = 92%



Completion rate did not change over time.



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Regulatory bodies demand accessibility, sponsors ask for the functionality

Important to preserve data integrity

Enhancing the Diversity of Clinical Trial Populations

- Avoiding unnecessary exclusions
- Developing eligibility criteria so that trial participants will better reflect the population likely to use the drug
- Applying the recommendations to trials in rare diseases

Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments

- COAs selected should be fit-for-purpose, well-supported by evidence, not be a burden to the patient and explained why each endpoint is informative for the trial context

Functionality requirements to enable accessibility

Visual impairment

- Adjustable font size
- High contrast screens
- Adjustable brightness/dark mode
- Zoom in/zoom out feature

Hearing difficulties

- Ability to print
- Voice and language selection

Motor & dexterity difficulties

- Assistive touch
- Large-print keyboard/touchscreen/stylus

Cognitive difficulties

- Consistent use of terminology
- Visual guidance

“Ensuring high quality measurement is important for several reasons: measuring what matters to patients; being clear about what was measured; appropriately evaluating the effectiveness, tolerability, and safety of treatments; and avoiding misleading claims.” FDA, April 2023

In preparation for publication

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Participant and Site Training: Ways to engage patients

Training for investigators and patients recommended by FDA and EMA

EMA Append 2 Oncology PRO Guidance

“

- Appoint a **PRO trained and qualified person** responsible for PRO data collection in each study site;

  […] in order to ensure they understand the importance of PRO assessment and will be able to motivate their patients to complete the PRO instruments;

- Education and training of **patients** before completion of the questionnaire

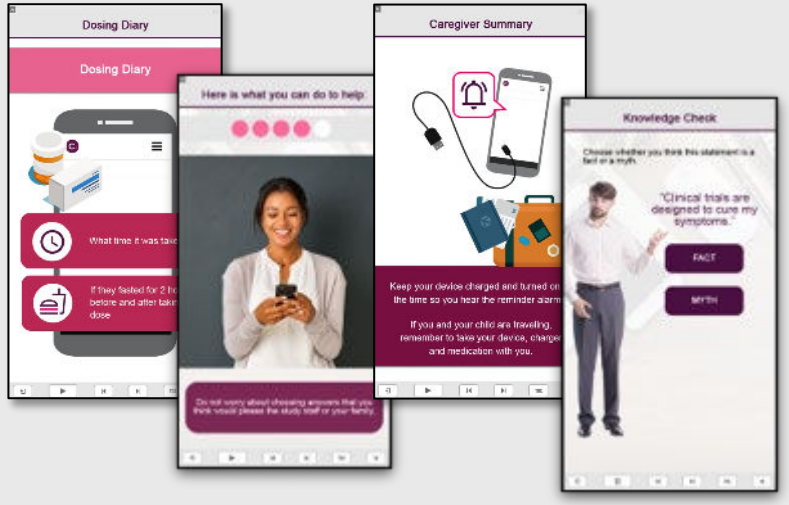
  […] including that there is no incorrect answer and explaining the purpose of the assessment.

  […] it should be carried out by means that do not influence the patient in their answers to the questionnaires themselves and it should be equally available to all patients participating in the project;

”

Keys for success:

- Easy accessible content
- Custom content
- Make it interactive
- Gating to eCOA assessments



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Key Takeaways

Use of PROs in oncology is increasing – Incorporating PROs in your oncology clinical trials is important for the **patient**, **regulators**, **drug differentiation**.

Continuing innovation to reduce burden and collect what matters to the patient is imperative – your PRO strategy **should reflect regulatory guidance and best practices**

Clinical trials are for the patient – **Leverage technology** to enhance accessibility and inclusion and increase engagement

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Thank you

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