National Cancer Institute's Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE™) Measurement System: An Overview

Sandra A. Mitchell, PhD, CRNP, FAAN
Senior Scientist and Program Director
Outcomes Research Branch
Healthcare Delivery Research Program

(sandra.mitchell@nih.gov)

NIH NATIONAL CANCER INSTITUTE
Division of Cancer Control & Population Sciences

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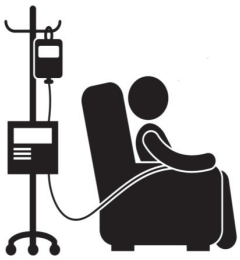
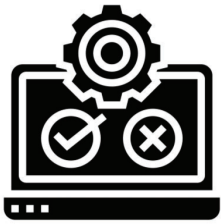
Overview and Background

Measuring Safety and Tolerability in Cancer Clinical Trials

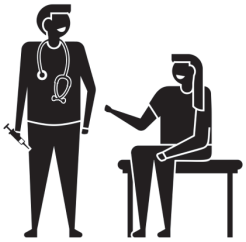


Safety and tolerability are fundamental to conclusions about the effectiveness of cancer therapies, including comparative effectiveness



In cancer clinical trials, adverse events are graded and reported using Common Terminology Criteria for Adverse Events (*CTCAE*) (now in version 5)

10% of the 800 adverse events listed in CTCAE are symptoms and thus are amenable to self-reporting



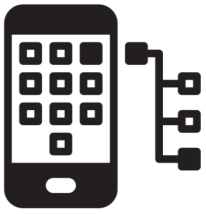
Validity of symptom reports may be eroded when filtered through research staff and clinicians[1]

Staff-based AE reporting occurs at clinic visits; AEs occurring between visits may be missed

[1]Xiao et al. (2013). *Cancer Nurs.*,36(6):E1-E16. doi: 10.1097/NCC.0b013e318269040f

Capturing Symptomatic Adverse Events Using Patient-Reported Outcomes

- Real-time ascertainment of symptomatic adverse events using PROs can improve the precision and reproducibility of adverse event reporting



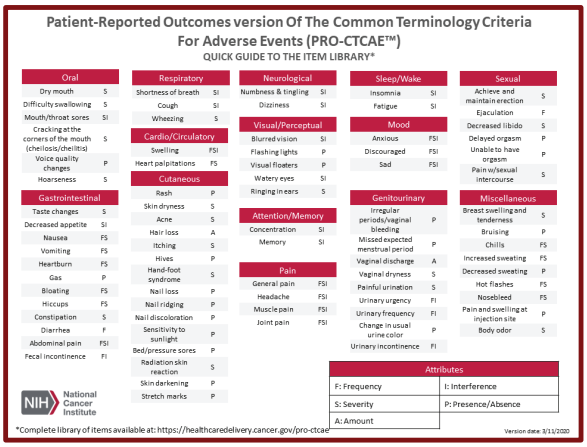
- **NCI's Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE™) Measurement System**
  - PRO measurement system developed to allow patient self-reporting of the presence/absence, frequency, severity and/or interference of symptomatic adverse events
  - Designed to be used as a companion to the CTCAE to capture the patient experience of symptomatic toxicities in cancer clinical trials

PRO-CTCAE™ Measurement System

- Symptomatic adverse events amenable to self-reporting were identified from CTCAE
- PRO-CTCAE items evaluate the symptom attributes of frequency, severity, interference, amount, presence/absence
- Conditional branching logic can be implemented with electronic data capture, thereby reducing respondent burden
- PRO-CTCAE linguistically validated in more than 40 languages
- Pediatric module permits self-reporting by children and adolescents ages 7-17 years (Ped-PRO-CTCAE™) or caregiver-reporting for children ages 7-17 who are unable to self-report (Ped-PRO-CTCAE™ [Caregiver])

PRO-CTCAE™ Measurement System

- Investigators select for prospective surveillance those PRO-CTCAE items that reflect anticipated symptomatic toxicities
- Custom surveys in more than 40 languages are created using the Form Builder function at the NCI PRO-CTCAE website



Patient-Reported Outcomes version Of The Common Terminology Criteria For Adverse Events (PRO-CTCAE™)

QUICK GUIDE TO THE ITEM LIBRARY*

Oral		Respiratory		Neurological		Sleep/Wake		Sexual	
Dry mouth	S	Shortness of breath	SI	Numbness & tingling	SI	Insomnia	SI	Achieve and maintain erection	S
Difficulty swallowing	S	Cough	SI	Dizziness	SI	Fatigue	SI	Ejaculation	F
Mouth/throat sores	SI	Wheezing	S					Decreased libido	S
Cracking at the corners of the mouth (cheilosis/chelitis)	S			Visual/Perceptual		Mood		Delayed orgasm	P
Voice quality changes	P	Cardio/Circulatory		Blurred vision	SI	Anxious	FSI	Unable to have orgasm	P
Hoarseness	S	Swelling	FSI	Flashing lights	P	Discouraged	FSI	Pain w/sexual intercourse	S
		Heart palpitations	FS	Visual floaters	P	Sad	FSI		
Gastrointestinal				Watery eyes	SI			Miscellaneous	
Taste changes	S	Cutaneous		Ringing in ears	S	Genitourinary		Breast swelling and tenderness	S
Decreased appetite	SI	Rash	P			Irregular periods/vaginal bleeding	P	Bruising	P
Nausea	FS	Skin dryness	S	Attention/Memory		Missed expected menstrual period	P	Chills	FS
Vomiting	FS	Acne	S	Concentration	SI	Vaginal discharge	A	Increased sweating	FS
Heartburn	FS	Hair loss	A	Memory	SI	Vaginal dryness	S	Decreased sweating	P
Gas	P	Itching	S			Painful urination	S	Hot flashes	FS
Bloating	FS	Hives	P	Pain		Urinary urgency	FI	Nosebleed	FS
Hiccups	FS	Hand-foot syndrome	S	General pain	FSI	Urinary frequency	FI	Pain and swelling at injection site	P
Constipation	S	Nail loss	P	Headache	FSI	Change in usual urine color	P	Body odor	S
Diarrhea	F	Nail ridging	P	Muscle pain	FSI	Urinary incontinence	FI		
Abdominal pain	FSI	Nail discoloration	P	Joint pain	FSI				
Fecal incontinence	FI	Sensitivity to sunlight	P						
		Bed/pressure sores	P						
		Radiation skin reaction	S						
		Skin darkening	P						
		Stretch marks	P						

Attributes	
F: Frequency	I: Interference
S: Severity	P: Presence/Absence
A: Amount	

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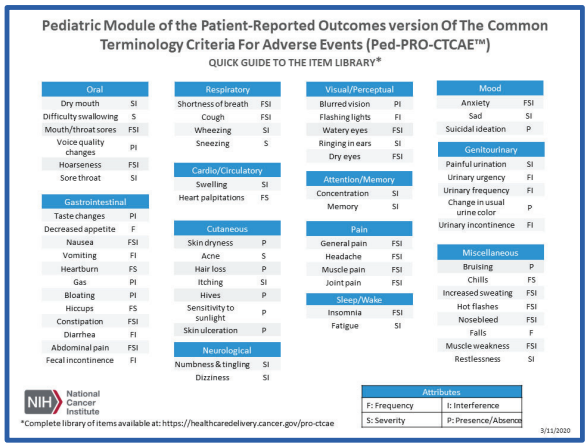
*Complete library of items available at: https://healthcaredelivery.cancer.gov/pro-ctcae

Version date: 3/11/2020



Pediatric Module of the Patient-Reported Outcomes version Of The Common Terminology Criteria For Adverse Events (Ped-PRO-CTCAE™)

QUICK GUIDE TO THE ITEM LIBRARY*

Oral		Respiratory		Visual/Perceptual		Mood	
Dry mouth	SI	Shortness of breath	FSI	Blurred vision	PI	Anxiety	FSI
Difficulty swallowing	S	Cough	FSI	Flashing lights	FI	Sad	SI
Mouth/throat sores	FSI	Wheezing	SI	Watery eyes	FSI	Suicidal ideation	P
Voice quality changes	PI	Sneezing	S	Ringing in ears	SI		
Hoarseness	FSI			Dry eyes	FSI	Genitourinary	
Sore throat	SI	Cardio/Circulatory				Painful urination	SI
		Swelling	SI	Attention/Memory		Urinary urgency	FI
Gastrointestinal		Heart palpitations	FS	Concentration	SI	Urinary frequency	FI
Taste changes	PI			Memory	SI	Change in usual urine color	P
Decreased appetite	F	Cutaneous				Urinary incontinence	FI
Nausea	FSI	Skin dryness	P	Pain			
Vomiting	FI	Acne	S	General pain	FSI	Miscellaneous	
Heartburn	FS	Hair loss	P	Headache	FSI	Bruising	P
Gas	PI	Itching	SI	Muscle pain	FSI	Chills	FS
Bloating	PI	Hives	P	Joint pain	FSI	Increased sweating	FSI
Hiccups	FS	Sensitivity to sunlight	P			Hot flashes	FSI
Constipation	FSI	Skin ulceration	P	Sleep/Wake		Nosebleed	FSI
Diarrhea	FI			Insomnia	FSI	Falls	F
Abdominal pain	FSI	Neurological		Fatigue	SI	Muscle weakness	FSI
Fecal incontinence	FI	Numbness & tingling	SI			Restlessness	SI
		Dizziness	SI				

Attributes	
F: Frequency	I: Interference
S: Severity	P: Presence/Absence

NIH National Cancer Institute

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3/11/2020

Patient-Reported Outcomes version Of The Common Terminology Criteria For Adverse Events (PRO-CTCAE™)

QUICK GUIDE TO THE ITEM LIBRARY*

Oral	
Dry mouth	S
Difficulty swallowing	S
Mouth/throat sores	SI
Cracking at the corners of the mouth (cheilosis/cheilitis)	S
Voice quality changes	P
Hoarseness	S

Gastrointestinal	
Taste changes	S
Decreased appetite	SI
Nausea	FS
Vomiting	FS
Heartburn	FS
Gas	P
Bloating	FS
Hiccups	FS
Constipation	S
Diarrhea	F
Abdominal pain	FSI
Fecal incontinence	FI

Respiratory	
Shortness of breath	SI
Cough	SI
Wheezing	S

Cardio/Circulatory	
Swelling	FSI
Heart palpitations	FS

Cutaneous	
Rash	P
Skin dryness	S
Acne	S
Hair loss	A
Itching	S
Hives	P
Hand-foot syndrome	S
Nail loss	P
Nail ridging	P
Nail discoloration	P
Sensitivity to sunlight	P
Bed/pressure sores	P
Radiation skin reaction	S
Skin darkening	P
Stretch marks	P

Neurological	
Numbness & tingling	SI
Dizziness	SI

Visual/Perceptual	
Blurred vision	SI
Flashing lights	P
Visual floaters	P
Watery eyes	SI
Ringing in ears	S

Attention/Memory	
Concentration	SI
Memory	SI

Pain	
General pain	FSI
Headache	FSI
Muscle pain	FSI
Joint pain	FSI

Sleep/Wake	
Insomnia	SI
Fatigue	SI

Mood	
Anxious	FSI
Discouraged	FSI
Sad	FSI

Genitourinary	
Irregular periods/vaginal bleeding	P
Missed expected menstrual period	P
Vaginal discharge	A
Vaginal dryness	S
Painful urination	S
Urinary urgency	FI
Urinary frequency	FI
Change in usual urine color	P
Urinary incontinence	FI

Sexual	
Achieve and maintain erection	S
Ejaculation	F
Decreased libido	S
Delayed orgasm	P
Unable to have orgasm	P
Pain w/sexual intercourse	S

Miscellaneous	
Breast swelling and tenderness	S
Bruising	P
Chills	FS
Increased sweating	FS
Decreased sweating	P
Hot flashes	FS
Nosebleed	FS
Pain and swelling at injection site	P
Body odor	S

Attributes	
F: Frequency	I: Interference
S: Severity	P: Presence/Absence
A: Amount	

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*Complete library of items available at: https://healthcaredelivery.cancer.gov/pro-ctcae

Version date: 3/11/2020

PRO-CTCAE™ Attributes and Item Structures

Frequency	Severity	Interference	Amount	Presence/Absence
In the last 7 days, how often did you have _____?	In the last 7 days, what was the severity of your _____ at its worst?	In the last 7 days, how much did _____ interfere with your usual or daily activities?	In the last 7 days, did you have any _____?	In the last 7 days, did you have any _____?
• Never • Rarely • Occasionally • Frequently • Almost constantly	• None • Mild • Moderate • Severe • Very severe	• Not at all • A little bit • Somewhat • Quite a bit • Very much	• Not at all • A little bit • Somewhat • Quite a bit • Very much	• No • Yes

- Each symptomatic AE is assessed by 1-3 attributes
- Conditional branching logic within PRO-CTCAE items can be implemented when using electronic data capture, thereby reducing respondent burden

CTCAE vs. PRO-CTCAE™ Item Structures

CTCAE					
Adverse Event	Grade				
	1	2	3	4	5
Mucositis oral	Asymptomatic or mild symptoms; intervention not indicated	Moderate pain; not interfering with oral intake; modified diet indicated	Severe pain; interfering with oral intake	Life-threatening consequences; urgent intervention indicated	-

PRO-CTCAE
Please think back over the past 7 days:
What was the severity of your MOUTH OR THROAT SORES at their WORST? None / Mild / Moderate / Severe / Very severe
How much did MOUTH OR THROAT SORES interfere with your usual or daily activities? Not at all / A little bit / Somewhat / Quite a bit / Very much

Pediatric PRO-CTCAE™(Ped-PRO-CTCAE™)

- Ped-PRO-CTCAE is comprised of questions that can be used to evaluate 62 symptomatic AEs drawn from the CTCAE
- Ped-PRO-CTCAE permits:
  - Self-reporting by children and adolescents ages 7-17 years (Ped-PRO-CTCAE™)
  - Caregiver-reporting by a parent or guardian when children or adolescents ages 7 to 17 years of age are unable to self-report (Ped-PRO-CTCAE™ [Caregiver])

Pediatric Module of the Patient-Reported Outcomes version Of The Common Terminology Criteria For Adverse Events (Ped-PRO-CTCAE™)

QUICK GUIDE TO THE ITEM LIBRARY*

Oral	
Dry mouth	SI
Difficulty swallowing	S
Mouth/throat pain	FSI
Voice quality changes	PI
Hoarseness	FSI
Sore throat	SI

Gastrointestinal	
Taste changes	PI
Decreased appetite	F
Nausea	FSI
Vomiting	FI
Heartburn	FS
Gas	PI
Bloating	PI
Hiccups	FS
Constipation	FSI
Diarrhea	FI
Abdominal pain	FSI
Fecal incontinence	FI

Respiratory	
Shortness of breath	FSI
Cough	FSI
Wheezing	SI
Sneezing	S

Cardio/Circulatory	
Swelling	SI
Heart palpitations	FS

Cutaneous	
Skin dryness	P
Acne	S
Hair loss	P
Itching	SI
Hives	P
Sensitivity to sunlight	P
Skin ulceration	P

Neurological	
Numbness & tingling	SI
Dizziness	SI

Visual/Perceptual	
Blurred vision	PI
Flashing lights	FI
Watery eyes	FSI
Ringing in ears	SI
Dry eyes	FSI

Attention/Memory	
Concentration	SI
Memory	SI

Pain	
General pain	FSI
Headache	FSI
Muscle pain	FSI
Joint pain	FSI

Sleep/Wake	
Insomnia	FSI
Fatigue	SI

Mood	
Anxious	FSI
Sad	SI
Suicidal ideation	P

Genitourinary	
Painful urination	SI
Urinary urgency	FI
Urinary frequency	FI
Change in usual urine color	P
Urinary incontinence	FI

Miscellaneous	
Bruising	P
Chills	FS
Increased sweating	FSI
Hot flashes	FSI
Nosebleed	FSI
Falls	F
Muscle weakness	FSI
Restlessness	SI

Attributes	
F: Frequency	I: Interference
S: Severity	P: Presence/Absence

NIH National Cancer Institute

*Complete library of items available at: https://healthcaredelivery.cancer.gov/pro-ctcae

2/7/2021

Ped-PRO-CTCAE™: Attributes and Item Structures

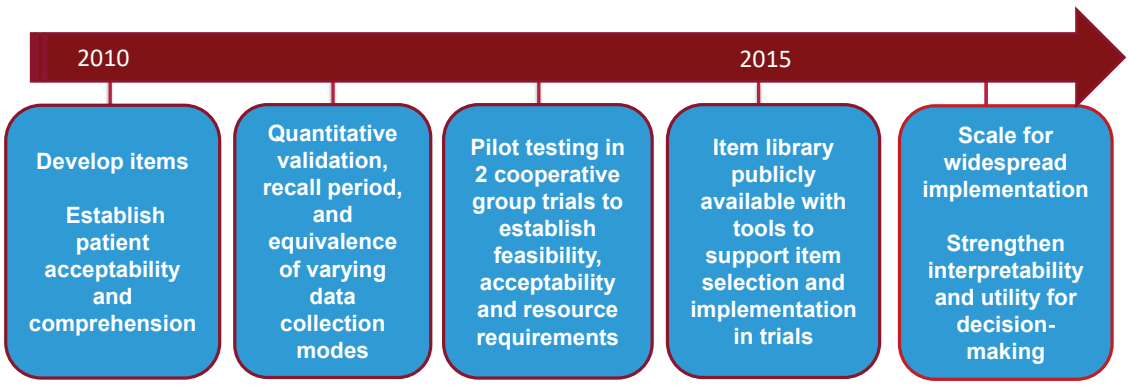
Frequency	Severity	Interference	Presence/Absence
How often did you have _____?	How bad was your _____?	How much did _____ keep you from doing things you usually do?	Did you have _____?
• Never • Sometimes • Most of the time • Almost all the time	• Did not have any • A little bad • Bad • Very bad	• Not at all • Some • A lot • A whole lot	• No • Yes • I do not know

- Recall period is the past 7 days
- Each symptomatic AE is assessed by 1-3 attributes
- Conditional branching logic within PRO-CTCAE items can be implemented when using electronic data capture, thereby reducing respondent burden
- Ped-PRO-CTCAE [Caregiver] employs comparable attributes; phrasing of items for caregiver-reporting replaces “you” with “your child”

PRO-CTCAE™
Development and Measurement Properties

PRO-CTCAE™ Measurement System

- Psychometrically robust library of items
- Accommodate diverse linguistic preferences
- Permit self-reporting by respondents across the developmental spectrum
- Supply meaningful data to improve understanding of symptomatic AEs



PRO-CTCAE™:Content Validity

Objective:

- Develop the items and examine the content validity of the PRO-CTCAE item library

Methods:

- Trialists, clinical experts, PRO methodologists, patient advocates, and representatives from the US Food and Drug Administration identified symptomatic AEs that can be meaningfully self-reported by patients[1]
- Three rounds of semi-structured cognitive interviews were conducted to evaluate comprehension, clarity and ease of judgement (N=127)[2]
- PRO-CTCAE items were iteratively refined between interview rounds

[1]Basch et al. (2014). *JNCI.*, 106(9). pii: dju244. doi: 10.1093/jnci/dju244
[2]Hay et al. (2014). *Quality of Life Research.*, 23(1):257-269. doi: 10.1007/s11136-013-0470-1

PRO-CTCAE™:Content Validity

Results:

- 78 symptomatic AEs identified from the more than 800 terms in the CTCAE lexicon; plain-language symptomatic AE terminologies developed[1]
- Each symptomatic AE term is assessed using 1 to 3 items[1]
- Frequency, severity, interference w/ daily activities, presence/absence, amount
- Cognitive interviewing using structured and open-ended probes (N=127)
  - 63/80 symptom terms generated no cognitive difficulties; 17 modified and re-tested without further comprehension difficulties[2]

[1]Basch et al. (2014). *JNCI.*, 106(9). pii: dju244. doi: 10.1093/jnci/dju244
[2]Hay et al. (2014). *Quality of Life Research.*, 23(1):257-269. doi: 10.1007/s11136-013-0470-1

PRO-CTCAE™: Validity and Reliability

Objective:

- Evaluate the quantitative measurement properties of PRO-CTCAE, specifically validity, reliability, sensitivity, and mode equivalence[1]

Methods:

- 975 patients who had received cancer-directed therapy in the prior two weeks were recruited and completed PRO-CTCAE surveys and EORTC QLQ C30
  - Convergent validity: associations with EORTC QLQ C30 scores
  - Known-groups validity based on disease site, clinical characteristics, and ECOG PS
  - Test-retest reliability: assessed on consecutive days in a subsample
- Sample was diverse with respect to age, disease site, and performance status:
  - 59 years (range 19-91); 82% White; 32%< high school; 35% lung/head and neck; 28% breast; 18% GU/Gyn; 17% PS 2-4

[1]Dueck AC et al. (2015). *JAMA Oncology.*, 1(8):1051-9. doi: 10.1001/jamaoncol.2015.2639

PRO-CTCAE™: Validity and Reliability

Results:

- PRO-CTCAE exhibits favorable validity, reliability, and responsiveness[1,2]
- Most PRO-CTCAE items (118/124) reached a statistically significant ($p<.05$) and meaningful effect size on one or more a priori validity criteria
- 6 items (rare events with low endorsement) could not be meaningfully validated in this sample
- All PRO-CTCAE items were associated with conceptually-relevant EORTC QLQ-C30 domains
- 96/124 PRO-CTCAE items distinguished subgroups based on performance status, disease site, and/or treatment characteristics

[1]Dueck AC et al. (2015). *JAMA Oncology.*, 1(8):1051-9. doi: 10.1001/jamaoncol.2015.2639
[2]Atkinson TM et al. (2018). *J Pain Symptom Manage.*,55(3):e3-e6. doi: 10.1016/j.jpainsymman.2017.10.024

PRO-CTCAE™: Validity and Reliability

Results:

- Acceptable test-retest reliability exhibited across subset of items tested (Median ICC 0.77)
- Response choices are well comprehended; each of the ordinal response choices is nonoverlapping and distinguishes respondents with meaningfully different symptom experiences

[1]Dueck AC et al. (2015). *JAMA Oncology.*, 1(8):1051-9. doi: 10.1001/jamaoncol.2015.2639
[2]Atkinson TM et al. (2018). *J Pain Symptom Manage.*,55(3):e3-e6. doi: 10.1016/j.jpainsymman.2017.10.024

PRO-CTCAE™: Mode Equivalence

- N=112 patients completed 28 PRO-CTCAE items (14 symptomatic A/Es) by each of the three modes of administration at a single clinic visit
- Average time to complete an item:
  - Web: 11.1 seconds (SD = ±8.4)
  - Interactive Voice Response (IVRS): 16.3 seconds (SD = ±6.3)
  - Paper: 10.3 seconds (SD = ±5.8)

Between modes, item-level mean differences were very small, and the corresponding effect sizes were all less than 0.20

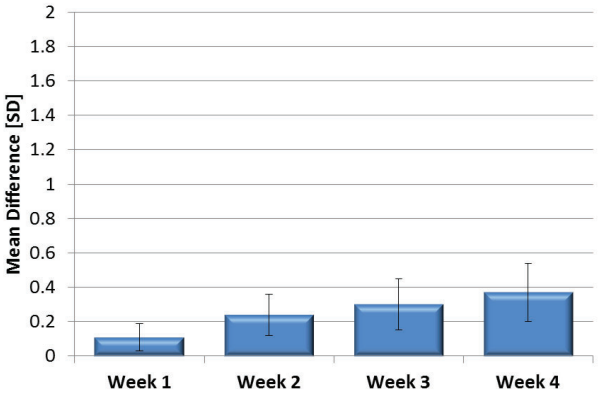
	Median ICC (Range)	Median (range) between-mode item-level mean difference
Web vs IVRS	0.78 (0.56 - 0.90)	-0.04 (-0.16 - 0.22)
Web vs paper	0.81 (0.61 - 0.96)	-0.02 (-0.11 - 0.14)
IVRS vs paper	0.78 (0.59 - 0.91)	0.02 (-0.07 - 0.19)

Bennett et al. (2016). *Health and Quality of Life Outcomes.*,19;14:24.doi: 10.1186/s12955-016-0426-6

PRO-CTCAE™:Comparison of Recall Periods

- N=110 patients completed 27 PRO-CTCAE™ items (14 symptomatic A/Es)
  - Comparison of 28 daily ratings to 1-, 2-, 3-, and 4-week recalled ratings
  - Mean difference between the average daily score and recalled score

1-week recall corresponds well to daily reporting. Differences between daily and longer recall periods widen with 2-, 3-, and 4-week recall



Mendoza et al. (2017). *Clinical Trials*., 14(3):255-263. doi: 10.1177/1740774517698645.

PRO-CTCAE™ Development Team

Sandra Mitchell (NCI) Ethan Basch (MSKCC) Amy Abernethy Jeff Abrams Angela Acevado Suneel Allareddy Benjamin Arnold Pamela Atherton Thomas Atkinson Melissa Barragán Natalie Barragán Paul Baumgartner Lauren Becker Antonia Bennett Nancy Breen Deborah Bruner Laurie Burke Kate Castro David Cella Sylvia Chou Ram Chilukuri Steven Clauser Charles Cleeland	Catherine Coleman Stephanie Consoli Maria Corona Cori Couture Gitana Davila Amylou Dueck Jana Eisenstein Maria Fawzy Shanda Finnigan Steve Friedman Joshua Gagne Vinay Gangoli Marcha Gatewood Araceli Garcia-Gonzalez Ann Geiger Cindy Geoghegan Venus Ginés Maria Gonzalez Mehul Gulati Gaurav Gupta Jay Harness Jennifer Hay Madeline Hernandez-Krause Lori Hudson Percy Ivy	Tony Kerlavage Warren Kibbe Paul Kluetz Reshma Koganti Virginia Kwitkowski Pauline Le Suzanne Lechner Lauren Lent Yuelin Li Carol Lowenstein Donna Malveaux Mauricio Medina Michael Mejia Tito Mendoza Michael Montello Cuong Nguyen Hannah O'Gorman Ann O'Mara Diane Paul John Payne Frank Penedo Barbara Perez Edgardo Ramirez Katherine Ramsey Bryce Reeve Lauren Rogak	Dave Rothfarb Sean Ryan Michael Sanchez Daniel Satele Martin Schoen Deborah Schrag Ann Setser Mary Shaw Sherri Sheinfeld-Gorin Marwan Shouery Laura Sit Jeff Sloan Ashley Wilder Smith Diane St. Germain Liora Stark Ann Marie Trentascosti Ted Trimble Andy Trotti Veronica Valenzula Andrea Vinard Vish Viswanath Amy Vito Gordon Willis Jennifer Wind

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PRO-CTCAE™ in Cancer Clinical Trials: Study Design, Analysis and Interpretation

Study Design Considerations

- PRO-CTCAE is designed to be used in conjunction with CTCAE
  - Provides complimentary information
  - Timing of assessments should be comparable and data reported in parallel
- Item selection and timing of assessment are critical design decisions to reduce risk of bias and maximize interpretability and utility of results
- Study design and analysis plan should consider published guidelines for protocol development and statistical analysis of studies that include a patient-reported outcome[1,2]

[1]Calvert et al. (2018). JAMA. 2018 Feb 6;319(5):483-494. doi: 10.1001/jama.2017.21903.
[2]Coens et al. (2020). Lancet Oncol. 21(2):e83-e96. doi: 10.1016/S1470-2045(19)30790-9.

Study Design Considerations

- Which toxicities to be measured?
  - Based on CTCAE-graded toxicities observed in earlier phase studies of agent, knowledge of drug class, and anticipated on- and off-target effects; qualitative work in the population (if it exists); input from investigators
  - Consistent with CAEPR as presented in the study protocol
  - Same PRO-CTCAE items in both study arms
  - Thoughtful item selection to minimize patient burden
- At what time points of measurement?
  - Baseline, regular intervals during treatment, at treatment discontinuation
  - Toxicity surveillance using CTCAE and PRO-CTCAE™ elements should reflect comparable timeframes

Study Design Considerations

- Planned analysis (descriptive and graphical)
- Inclusion of back-up data collection strategies and real-time monitoring of data quality to limit missing data
- Free-text write-ins for unsolicited symptoms

Interpretation and Reporting

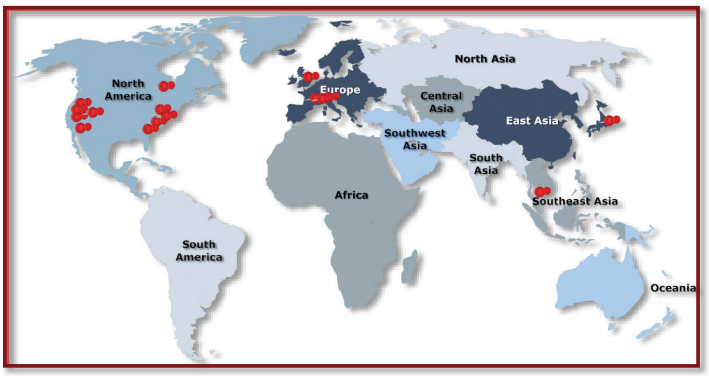
- PRO-CTCAE Score ≠ Clinician CTCAE Grade
- Up to three patient-reported scores per symptomatic toxicity
- Best way to combine the attributes (frequency, severity, interference) and to interpret the scores has not been established and is under study
- CTCAE Grade 4 does not exist for most of the PRO-CTCAE toxicities
- Descriptive reporting of available attributes is recommended
- Significant additional scientific study focused on validity and interpretabilty is needed before individual-level PRO-CTCAE scores can be used for clinical and protocol-specific decision-making (e.g. dose adjustments)
- PRO-CTCAE data is not included in FDA clinical site inspections or IND safety reporting, but descriptive findings, and missing data/data quality should be available for review by the DSMB

Kim et al. Use of PRO Measures to Inform Tolerability in Oncology Trials: Implications for Clinical Review, IND Safety Reporting, and Clinical Site Inspections. *Clin Cancer Res*. 2018 Apr 15;24(8):1780-1784

PRO-CTCAE™
Continued Development and Future Directions

Expanding Adoption and Implementation

- Collaborations with leading national and international organizations to enhance uptake and adoption in clinical trials
  - NCI National Clinical Trials Network (NCTN) and Early Therapeutics Clinical Trials Network (ETCTN)
  - Regulatory: US Food and Drug Administration, NHS in UK, EMA
  - International: Italian NCI, Japanese NCI, Danish Cancer Society, German Society of Hematology and Medical Oncology (DGHO)



- PRO-CTCAE has been linguistically validated in more than 40 languages; 20 additional languages currently in development and validation
- Pediatric module available in English, Italian and Chinese; additional validation studies ongoing

Strengthening Interpretability and Clinical Utility

- Interpretation and clinical utility of PRO-CTCAE still evolving
  - Continued implementation in early phase trials, precision medicine studies and randomized trials
  - Anticipate future novel trial designs incorporating PRO-CTCAE data in real time for dose-finding and tailoring therapy for vulnerable subgroups
- Ongoing work to enhance interpretability and utility of PRO-CTCAE
  - Empirically-derived mapping of PRO-CTCAE item scores into CTCAE grades using a discrete choice methodology to establish IRT metric
  - Adopters in surgical oncology, immuno-oncology, and radiation oncology testing items to expand the item library
  - Additional languages undergoing linguistic validation through a series of CRADAs
  - Evaluate different approaches to patient-investigator grade reconciliation and to analyzing and representing PRO-CTCAE data and strengthening the analysis and interpretation of PRO-CTCAE and CTCAE data jointly, thereby improving our understanding of treatment tolerability

Improving our Understanding of the Tolerability of Cancer Treatments

- PRO reporting of symptomatic adverse events is
  - Crucial to patients, their clinicians, trial sponsors, and regulators
  - Essential to determinations of benefit and harm at the study level
- PRO-CTCAE will ultimately be interpreted within the CTCAE reporting framework
- Ongoing efforts to embed PRO-CTCAE into cancer treatment trials and observational studies will provide
  - Understanding of how reporting could influence dose modifications
  - Evidence-based principles for PRO-CTCAE-related study design and trial workflow
  - Understanding of treatment tolerability as an endpoint that is interpretable and useful for decision-making at both the individual and trial-level

For more information about the PRO-CTCAE™ Measurement System visit:
https://healthcaredelivery.cancer.gov/pro-ctcae

Questions?