The PRO-CTCAE to Understand Symptomatic Toxicities with Cancer Medication: An American Dream or a Global Opportunity

Moderator

Matthew Reaney

Panelists

Olivier Chassany

Tony Dhillon

Eva Susanne Dietrich

Agenda for PRO-CTCAE Panel

+ Topic introduction by panel moderator
+ Panel discussion
+ Q&A

Efficacy data in oncology clinical trials has long included patient-reported outcomes, but safety data has relied on clinician report

Efficacy

- Survival
- Progression
- Functioning improvement (e.g., FACT-G)
- Symptom deterioration (e.g., EORTC QLQ-C30)
- Health status/Quality of Life maintenance (e.g., EQ-5D)

Safety

- Adverse Events (CTCAE)
- Serious Adverse Events (CTCAE)

Patient-reported treatment-induced symptoms?

Tolerability of treatment

Acceptability of/satisfaction with treatment

Adherence

FDA recommends focusing on five core concepts across oncology indications to capture meaningful patient experiences

Core Concepts

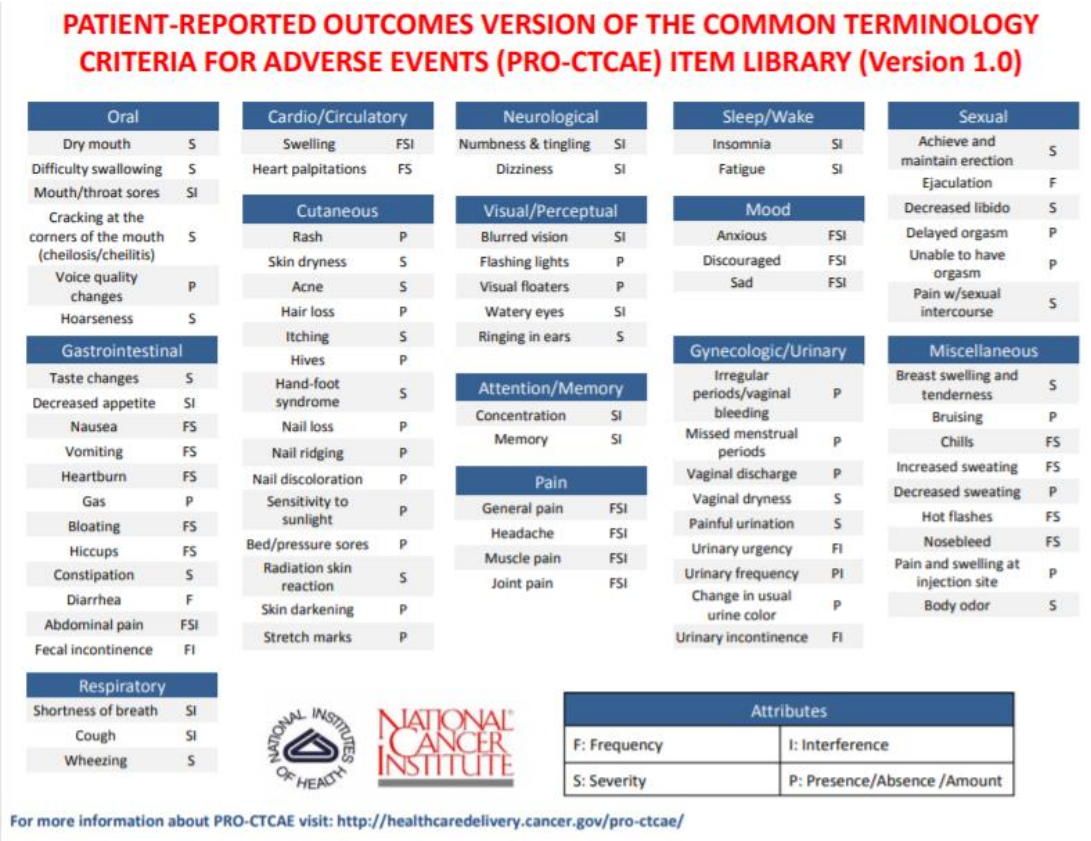
- Disease-Related Symptoms
- Symptomatic Adverse Events
- Overall Side Effect Impact Summary Measure
- Physical Function
- Role Function

> *FDA recommends selecting a concise set of the most important symptomatic AEs that are expected to occur from an item library…* ***FDA considers the … (PRO-CTCAE) to be an example of one acceptable item library for assessment of symptomatic adverse events.***

Source: U.S. Department of Health and Human Services Food and Drug Administration Oncology Center of Excellence (OCE), Center for Drug Evaluation and Research (CDER), and Center for Biologics Evaluation and Research (CBER). June 2021. Core Patient-Reported Outcomes in Cancer Clinical Trials, Guidance for Industry, DRAFT GUIDANCE. Available at https://www.fda.gov/media/149994/download

The PRO-CTCAE is a PRO measurement system developed by the NCI to capture patient-reported AEs and treatment-related symptoms

- The PRO-CTCAE item library includes 124 items representing 78 symptoms drawn from the CTCAE, the standard lexicon for AE reporting in cancer clinical trials
- Items evaluate the symptom attributes of frequency, severity, interference, amount, and/or presence absence
  - Each symptomatic AE is assessed by one to three attributes
- Broad range of potential uses



PATIENT-REPORTED OUTCOMES VERSION OF THE COMMON TERMINOLOGY CRITERIA FOR ADVERSE EVENTS (PRO-CTCAE) ITEM LIBRARY (Version 1.0)

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	P
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

Gynecologic/Urinary	
Irregular periods/vaginal bleeding	P
Missed menstrual periods	P
Vaginal discharge	P
Vaginal dryness	S
Painful urination	S
Urinary urgency	FI
Urinary frequency	PI
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 /Amount

For more information about PRO-CTCAE visit: http://healthcaredelivery.cancer.gov/pro-ctcae/

AE: Adverse event | CTCAE: Common Terminology Criteria for Adverse Events | NCI: National Cancer Institute | PRO: Patient reported outcome | PRO-CTCAE: Patient-Reported Outcomes version of The Common Terminology Criteria for Adverse Events

PRO-CTCAE items include a varying number of attributes

17. PRO-CTCAE™ Symptom Term: Abdominal pain

a. In the last 7 days, how OFTEN did you have PAIN IN THE ABDOMEN (BELLY AREA)?

O Never	O Rarely	O Occasionally	O Frequently	O Almost constantly

b. In the last 7 days, what was the SEVERITY of your PAIN IN THE ABDOMEN (BELLY AREA) at its WORST?

O None	O Mild	O Moderate	O Severe	O Very severe

c. In the last 7 days, how much did PAIN IN THE ABDOMEN (BELLY AREA) INTERFERE with your usual or daily activities?

O Not at all	O A little bit	O Somewhat	O Quite a bit	O Very much

25. PRO-CTCAE™ Symptom Term: Skin dryness

a. In the last 7 days, what was the SEVERITY of your DRY SKIN at its WORST?

O None	O Mild	O Moderate	O Severe	O Very severe

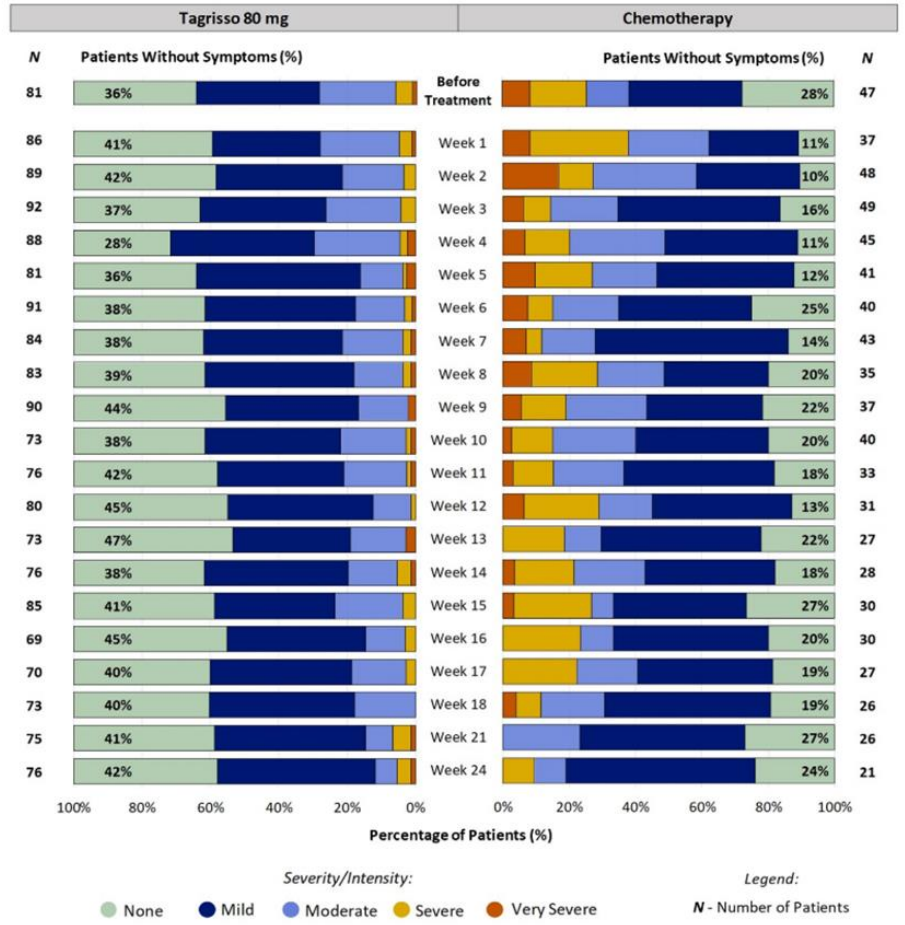
Source: NCI - PRO-CTCAE™ Items - English; Item Library Version 1.0 (cancer.gov)

FDA's pilot Project Patient Voice (PPV) developed as a source of PRO-CTCAE data accessible to patients, caregivers, and HCPs

Table 1. Summary of Symptom Frequency

Column A	Column B		Column C		Column D		Column E	
Symptom (Attribute)	No. of Patients[1]		Any symptom before treatment (%)[2]		Any Worsening on treatment (%)[3]		Worsening to Score 3 or 4 (%)[4]	
	Tagrisso	Chemo	Tagrisso	Chemo	Tagrisso	Chemo	Tagrisso	Chemo
Loose or Watery Stools (F)	80	44	31%	39%	70%	61%	19%	16%
Numbness or Tingling in Hands or Feet (S)	80	44	24%	30%	59%	50%	3%	7%
Pain in the Abdomen (F)	80	44	19%	43%	59%	61%	9%	14%
Fatigue, Tiredness or Lack of Energy (S)	80	44	64%	70%	58%	73%	24%	45%
Hand-Foot Syndrome (S)	80	44	31%	30%	54%	43%	5%	5%
Acne or Pimples on the Face or Chest (S)	80	44	36%	30%	53%	32%	0%	0%
Dry Mouth (S)	80	44	43%	43%	50%	68%	11%	20%
Mouth and Throat Sores (S)	80	44	21%	18%	48%	66%	9%	11%
Arm or Leg Swelling (F)	80	44	15%	20%	46%	45%	10%	16%
Itchy Skin (S)	80	44	48%	55%	46%	39%	5%	2%
Rash (O)	80	44	35%	20%	46%	34%	N/A	N/A
Dry Skin (S)	80	44	73%	77%	44%	34%	6%	2%
Nausea (F)	80	44	25%	32%	41%	77%	6%	39%
Blurry Vision (S)	80	44	29%	32%	39%	52%	3%	9%
Decreased Appetite (S)	80	44	54%	52%	39%	68%	10%	30%

Figure 1. Patient-Reported Fatigue During the First 24 Weeks on Treatment



This panel will discuss how the use of the PRO-CTCAE is likely to evolve in EU markets

Matthew Reaney, Panel Moderator
Global Science & Analytics Lead, Patient-Centered Solutions, IQVIA

- Chartered Practitioner Health Psychologist
- 15+ years industry experience in patient outcomes
- Senior scientific advisor to strategy and scientific projects at IQVIA on clinical outcome assessments and patient experience data
- Academic roles at 3 UK Universities
- Expert in PRO science and regulatory strategy; experience working with the PRO-CTCAE in clinical development

Panelists

Olivier Chassany
Professor of Therapeutics
- *Chair of ISPOR Clinical Outcomes Assessment SIG*
- *Researcher in Patient-Reported Outcomes, AP-HP & Université de Paris*
- *Past PRO expert of EMA, Ethics Committee member for 30 yrs*

Tony Dhillon
Consultant Medical Oncologist, Royal Surrey Hospital, UK
- *Oncologist at Royal Surrey County Hospital*
- *Key opinion leader in GI cancers and research*
- *Clinical trials investigator*
- *Fellow of Royal College of Physicians*

Eva Susanne Dietrich
Head of Institute for Evidence-Based Positioning in the Health Care Sector
- *Consultant, honorary professor University of Bonn, Germany*
- *Former deputy member of G-BA*
- *Former head of department of drugs at KBV*

The panel will include a discussion of 3 core questions

1. Do you see a role for PRO-CTCAE in your line of work?

2. Do you think its use with regulators, payers, and in clinical practice will increase as it gets implemented more and as people become more familiar with the data?

3. Would you advise drug and biologic developers to embrace the PRO-CTCAE in trials? What are the opportunities and risks?