CDDF Multi-stakeholder Workshop

Endpoints in Cancer Drug Development

Session 3: PRO Endpoints – Regulatory Perspective

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Disclosures

- I have no financial disclosures
- I will not be discussing off-label and/or investigational use of named products in this presentation
- These slides represent current thinking in a rapidly evolving field of regulatory science

Outline

- Identify pitfalls with commonly used patient-reported outcomes analyses
- Describe the FDA reviewer perspective when analyzing submitted PRO
- Highlight the OCE's core outcome set and optimal assessment frequency
- Consider how novel communication tools can be used to share useful PRO data to patients and providers

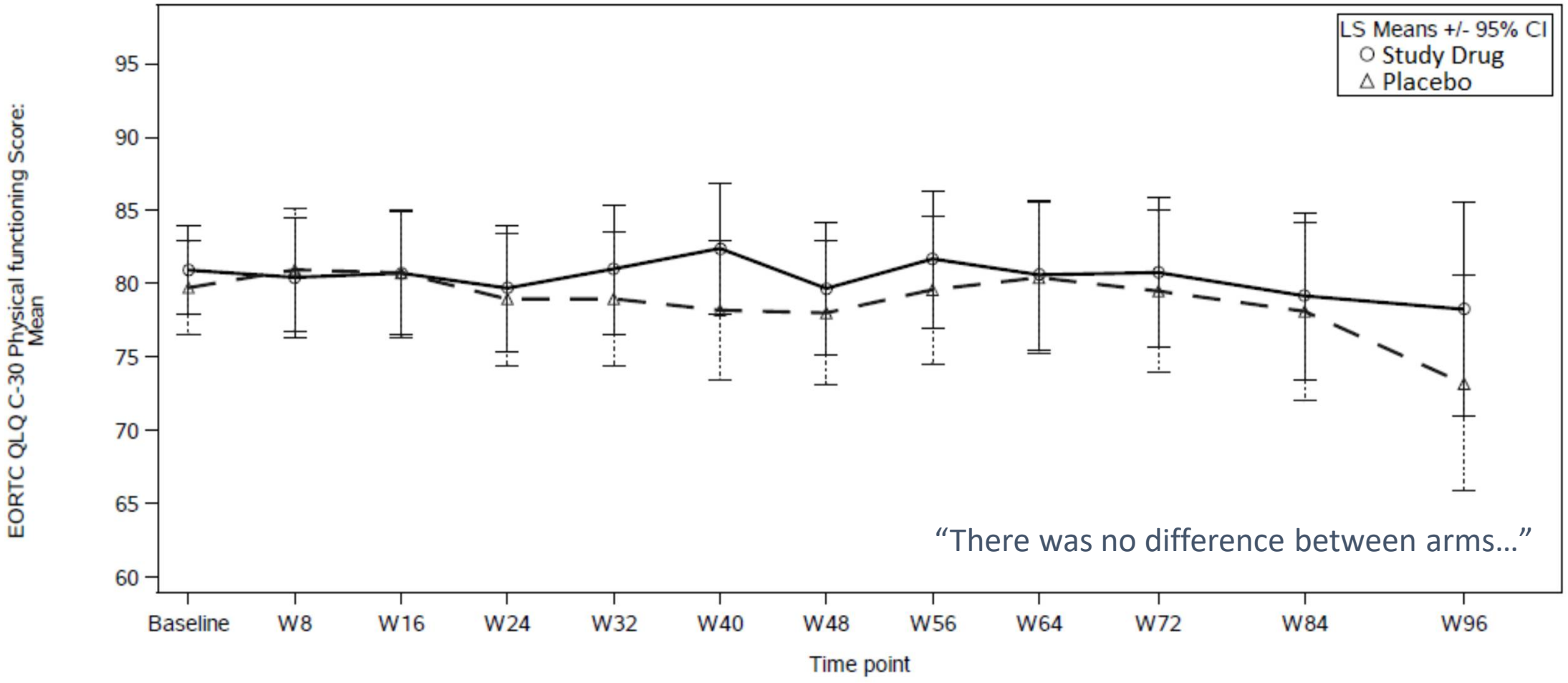
Challenges

21st Century Cures Act encourages FDA to review and communicate patient experience data submitted in product reviews

PRO data are frequently submitted; heterogeneity exists in analysis and presentation of data

Product label (USPI) offers limited space to communicate patient experience data adequately

Common Scenario



"There was no difference between arms…"

Review Strategy

- Which instruments are being used? Concepts proximal to disease?
- Are PRO descriptive (e.g. tolerability) or claims of treatment benefit?
- What confounders could limit interpretability of results?
- How much data is missing?
- Is the assessment timing reasonable given the drug(s) being tested?
- Can conclusion be made based on the strength of results?
- What are the implications for patients, caregivers and practitioners?
- What is the best way to share PRO data (results) with the public?

Core Outcomes

Overall Survival
Progression Free Survival
Overall Response Rate
Serum Biomarkers

CTCAE Safety Data
Dose Modifications

Hospitalizations
ED Visits
Morbid Procedures
Supportive Care Use

Clinician Reported and Biomarker Data

Disease Symptoms

Symptomatic Adverse Events

Overall Side Effect Impact

Physical Function:

Ability to Carry Out Activities that Require Physical Effort

Role Function:

Ability to Work and Perform Leisure Activities

Patient Generated Data

PRO Core Outcomes Assessment Frequency

	Standard 6 month treatment period												Follow-up	
	BL	w2	w3	w4	w5	w6	w7	w8	M3	M4	M5	M6	M9	M12*
Symptomatic AE	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

***Assessments at further timepoints would be context dependent**

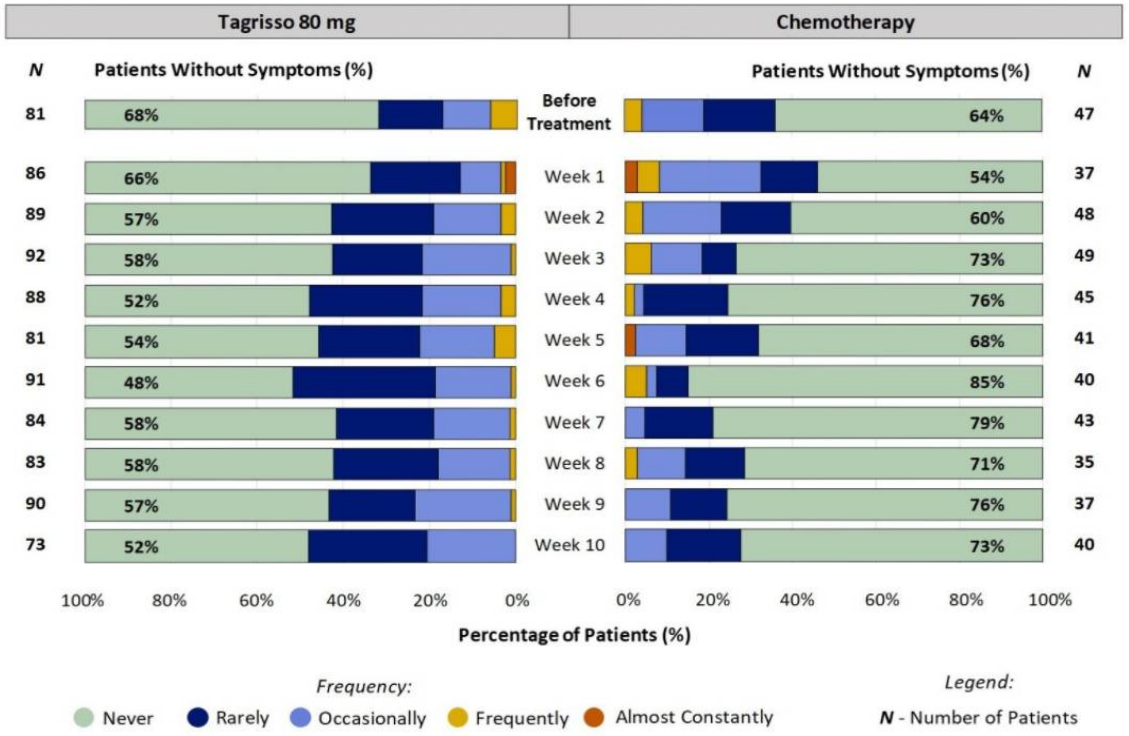
Additional relevant items outside of the Core Outcomes may be necessary depending on the context (e.g. swallowing fxn, xerostomia in a head and neck cancer trial)

Communication is Key!

Patient-Reported Diarrhea During the First 24 Weeks on Treatment for Patients Who Completed a Questionnaire:

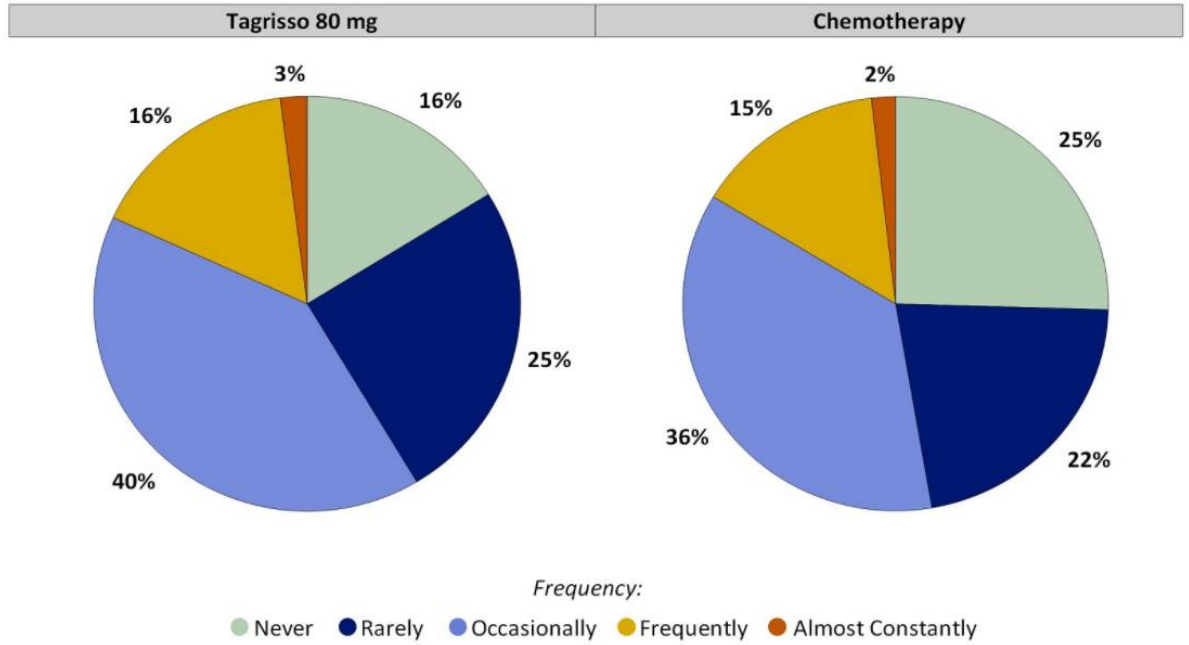
Figure 1 shows the percentage of patients reporting how often they had Diarrhea at each time point. For example, at week 2, 43% of patients taking Tagrisso reported Diarrhea (ranging from Rarely to Frequently). The range of patients who had any Diarrhea during the first 24 weeks of treatment with Tagrisso was between 34% - 53%. Click here for more information on how to read the graphs below.

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



Worst Response Option for Diarrhea That Patients Reported During the First 24 Weeks on Treatment

Figure 2. Worst Patient-Reported Diarrhea During the First 24 Weeks on Treatment



https://www.fda.gov/about-fda/oncology-center-excellence/project-patient-voice

Conclusions

- Measurement of patient-reported disease symptoms every 3 months is not enough.
- Prospectively define PRO objectives, research questions and endpoints.
- Focus on key areas that are directly related to the disease/treatment being studied – e.g., for HNSCC consider focusing on swallowing function in addition to core outcomes.
- PRO data should be collected and analyzed in a way that's meaningful and interpretable for patients and providers.
- Consider alternative methods to collect patient experience in addition to traditional PRO: wearables, sensors, etc.

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