# Electronic Collection of Patient-Reported Outcomes (PROs) in NCI-sponsored Clinical Trials

*Lori Minasian, M.D.*

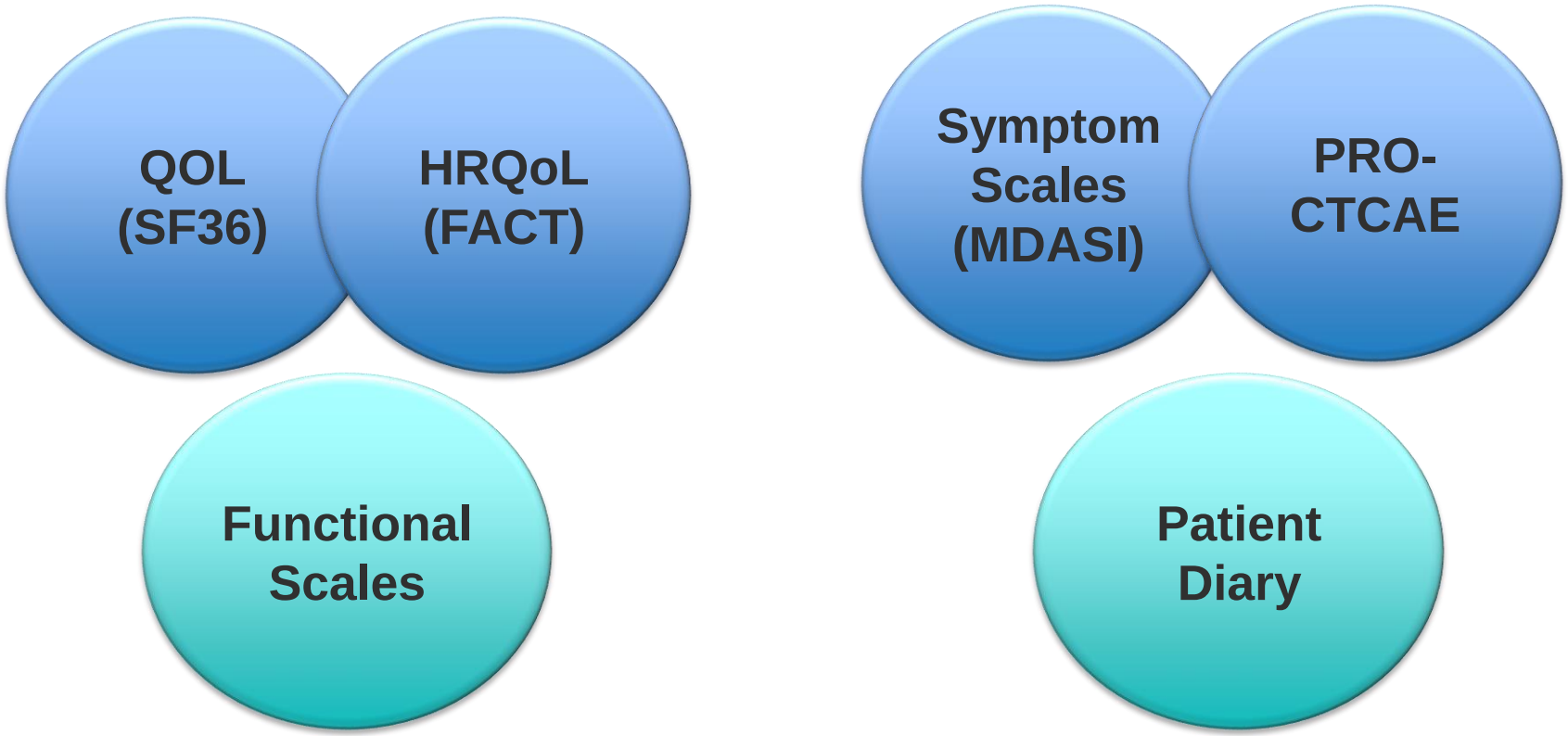
*Deputy Director, Division of Cancer Prevention*

NIH NATIONAL CANCER INSTITUTE

November 6, 2024

# Patient Reported Outcomes

***Any item reported by patients***



# Incorporating PROs in NCI Clinical Trials

Incorporate patient reported information into the study design to better identify safe and effective interventions to treat, prevent and control cancer.

- Improve our ability to identify tolerable regimens.
- Understand the patient experience and improve the ability for clinicians to communicate anticipated trajectory of symptoms and function to patients.

Improve operational efficiency for the collection of PROs for investigators and site staff.

- Streamline data collection and improve data quality.
- Facilitate the analysis by integration of PROs into the existing electronic data collection.

***Typically, patients are happy to provide their perspective but want the information to be used and useful.***

# Collection Methods for PROs

## Paper and pencil

- Long history of paper booklet collection
- Research staff enter patient responses into case report forms
- Paper booklet retained as source documentation

## Telephone

- Some Groups have used telephone collections

## Electronic

- Industry standard is electronic data capture
- 3 of the 4 adult NCTN Groups using some form of electronic PRO collection
- NCI pilot with Medidata ePRO tool:

*Accommodating multiple modalities is key to increasing participant diversity*

# NCI Efforts to Improve Efficiency of PRO Capture

NCI Pilot project with Medidata ePRO Module

- Pilot from 2016 to 2020 evaluated efficiency and operations.
- Mixed results: better data, but greater challenges for sites.
- Valuable learning experience:
  - Received specific feedback from end users.
  - Refined understanding of requirements.
  - Importance of CTSU integration.
  - Explored best practices for ePRO training and support.

# CTSU Integrated Solution

# Overarching Solution for Electronic PRO Collection

Integration with Cancer Trials Support Unit (CTSU)

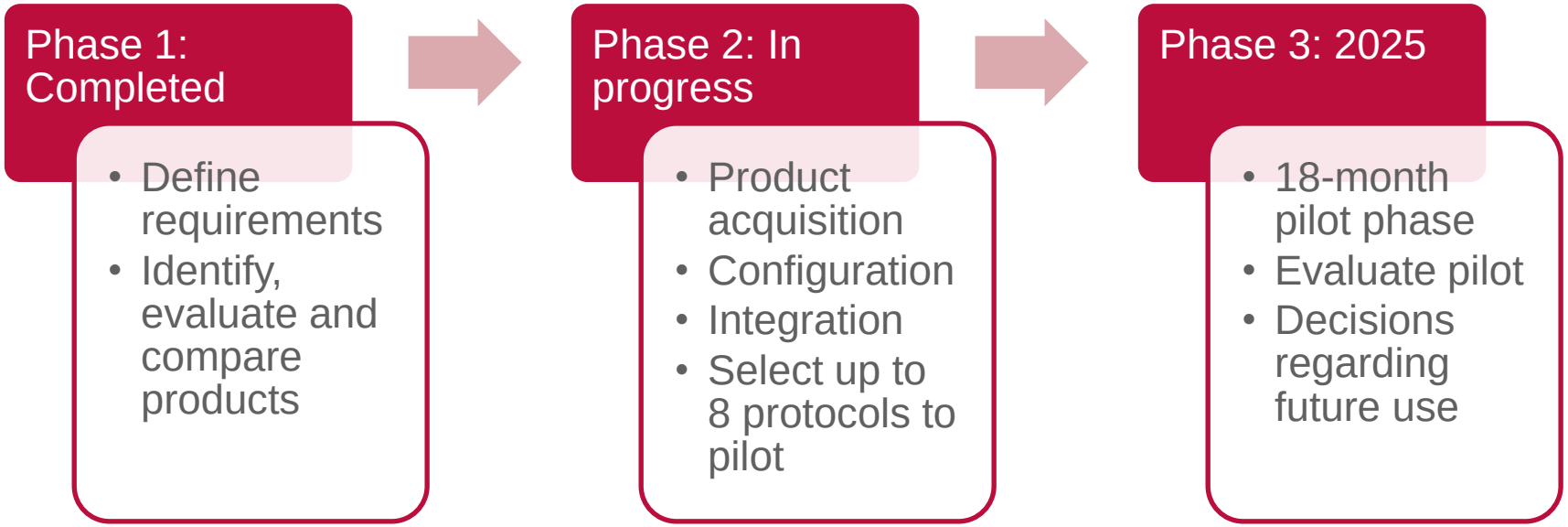
- CTSU coordinates all aspects of NCI clinical trials systems
  - Extramural clinical trials investigators do their work through CTSU
  - Provides standardized, integrated support services across networks
  - Improves efficiency and eliminates redundant processes
  - Currently handles the issues and challenges associated with ePRO

CTSU facilitates all the regulatory requirements

- Working to ensure compliance with the Clinical Data Interchange Standards Consortium (CDISC)
  - CDISC in the process of identifying the data standards for PROs

# CTSU Task Order: ePRO

Purpose: Identify, configure and pilot an ePRO platform for possible future NCI use



# Stakeholder-Driven Process

Multi-Center Organization Working Group

- 28 NCTN and NCORP Research Base Representatives
  - ePRO subject matter experts
  - Data management staff
  - Technical/data management
  - Statistics
- NCI staff from NCORP and NCTN
- Define and prioritize specific requirement
- Clarify workflows

# Stakeholder-Driven Process

- Site and Patient Representative Working Group
  - 9 site staff
  - 10 patient representatives

- Streamlining user experience
- Increase patient satisfaction
- Strategies to maximize adoption of ePRO
- Identify the benefits and drawbacks of specific ePRO platforms

# ePRO Platform Evaluation and Selection

- 25 potential platforms were identified
  - Scored based on publicly available information
- 9 top-scoring platforms
  - RFI used to obtain additional information
  - ROM costs
  - Real-time platform demonstration
- 5 top-scoring platforms
  - RFP: Technical response, pricing details, access to ‘sandbox’ testing
  - Scored based on quality of available evidence, satisfaction of requirements, qualitative results

# Platform for ePRO

# Final Selection: OpenClinica

- Top scoring platform
- Most robust RFP responses
- Most responsive of final vendors

# OpenClinica: Features and Benefits

Multi-Center Organizations

- Synchronization to Rave-based study calendar:
  - accommodates treatment or study delays, schedule changes.
- Flexibility to accommodate unique PRO needs of individual studies
- Access to item libraries and form templates
- Supports participation of non-English speakers
- Customized protocol-specific notifications and scheduled reminders
- ePRO completion monitoring across participants, sites, and trials
- Robust reporting capabilities by user type (such as MCO, NCI)

# OpenClinica: Features and Benefits

## Sites

- Uses existing NCI credentials for access (single sign-on)
- Automatic notifications to patients, including off-schedule situations
- Reporting capabilities
- Technical support, patient-facing help desk

## Participants

- Link-based access; no passwords to navigate
- Does not require patients to download an app
- Accessible from a PC, smartphone, or tablet
- Responses can be saved for later completion

# Next Steps for CTSU Task Order

## Ongoing

- Integrating with NCI systems
- System configuration
- Re-engaging working groups
- Training and Evaluation Plans

Pilot Study Characteristics

- PRO as primary or secondary endpoint
- Protocol contains multiple PROs
- Anticipated strong accrual
- Diversity of sites

## Pilot Phase: begins early 2025

- Up to 8 studies
- 18 months
- Evaluation: functionality, usability, acceptability, adoption

# Implementation of ePRO

# Implementation of ePRO through CTSU

Review results of pilot with OpenClinica

- Prioritize trials in which PROs are key endpoints
  - Trials with hypothesis driven incorporation of PROs to further inform the trial results
  - Trials in which PROs are the primary endpoint
  - Trials in which PROs are used to assess tolerability as key secondary endpoints

NCI-sponsored networks using CTSU may have access to ePRO platform for the collection of PROs in which a rigorous plan for collection and analysis is needed.

- Trials using PROs endpoints in the regulatory approval

# Increasing Use of PROs in Hematologic Malignancies

Update to Lancet Hematology Commission on Adverse Event Reporting (2024, under review)

- PROs contributed to better understanding of novel AML therapies
- PROs Incorporated into endpoints for myelofibrosis trials
- PROs can capture patient discontinuation of oral therapy due to early symptomatic adverse events
  - (CLL example O’Connell JCO 2024)

# PROs in the FDA-Approved Product Label

**HIGHLIGHTS OF PRESCRIBING INFORMATION**
**These highlights do not include all the information needed to use ITOVEBI safely and effectively. See full prescribing information for ITOVEBI.**

**ITOVEBI (inavolisib) tablets, for oral use**
**Initial U.S. Approval: 2024**

**Table 3: Adverse Reactions (≥ 10% with ≥ 5% [All Grades] or ≥ 2% [Grade 3-4] Higher Incidence in the ITOVEBI Arm) in INAVO120**

| Adverse Reaction | ITOVEBI + Palbociclib + Fulvestrant N=162 | | Placebo + Palbociclib + Fulvestrant N=162 | |
|---|---|---|---|---|
| | All Grades (%) | Grade 3-4 (%) | All Grades (%) | Grade 3-4 (%) |
| **Gastrointestinal Disorders** | | | | |
| Stomatitis[a] | 51 | 6* | 27 | 0 |
| Diarrhea | 48 | 3.7* | 16 | 0 |
| Nausea | 28 | 0.6* | 17 | 0 |
| Vomiting | 15 | 0.6* | 5 | 1.2* |
| **General Disorders and Administration Site Conditions** | | | | |
| Fatigue | 38 | 1.9* | 25 | 1.2* |
| **Skin and Subcutaneous Tissue Disorders** | | | | |
| Rash[b] | 26 | 0 | 19 | 0 |

**Table 5: Patient-Reported Symptoms Assessed by PRO-CTCAE in INAVO120**

| Symptom (Attribute)[a] | Any Symptom Before Treatment (%)[b] | | Any Worsening on Treatment (%)[c] | | Worsening to Score 3 or 4 (%)[d] | |
|---|---|---|---|---|---|---|
| | ITOVEBI + P + F (N=148)[e] | Placebo + P + F (N=152)[e] | ITOVEBI + P + F (N=148)[e] | Placebo + P + F (N=152)[e] | ITOVEBI + P + F (N=148)[e] | Placebo + P + F (N=152)[e] |
| Diarrhea (frequency), % | 23 | 15 | 78 | 49 | 32 | 8 |
| Nausea (frequency), % | 21 | 21 | 59 | 50 | 20 | 11 |
| Vomiting (frequency), % | 9 | 6 | 35 | 26 | 6 | 3.3 |

# Summary

- PROs can provide complimentary information when captured rigorously
- Electronic capture of PROs can help with the rigorous collection of PROs, but needs to be feasible
- Through the CTSU, NCI is piloting the electronic capture of PROs using OpenClinica platform
  - Selected studies will be identified for the pilot phase
  - Use of the ePRO platform will be prioritized for those trials in which the PROs are intended as key endpoints

# Thank You


cancer.gov

cancer.gov/espanol