Lessons Learned: Challenges and Wins

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PRO Consortium Co-Director

THIRD ANNUAL
PATIENT-REPORTED OUTCOME (PRO) CONSORTIUM WORKSHOP

April 4, 2012 ■ Silver Spring, MD

Co-sponsored by

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FDA

Agenda

- ***Lessons Learned: Challenges and Wins***
  - ***Introduction*** – Risa Hayes, PhD – Eli Lilly and Company
  - ***Asthma Working Group -*** Linda Nelsen, MHS – Merck Sharpe & Dohme
  - ***Depression Working Group -*** Steven I. Blum, MBA – Forest Research Institute
  - ***Functional Dyspepsia Working Group -*** Robyn T. Carson, MPH – Forest Research Institute
  - ***Irritable Bowel Syndrome Working Group -*** Mollie J. Baird, MPH – Ironwood Pharmaceuticals
  - ***Non-Small Cell Lung Cancer Working Group -*** Rajiv Mallick, PhD – Daiichi Sankyo
- ***FDA Response***
  - Laurie Beth Burke, RPh, MPH; Marc K. Walton, MD, PhD
- ***Open floor discussion***

A Consortium of Pharma

2011

- *Teleconferencing across 9 different time zones is only the beginning…*

2012

- ***Challenges:*** Time, member turnover, uncertainty, agendas
- ***Wins:*** Face-to-face meetings, non-competitive environment

Interactions with the FDA

2011

The good news and the not so good news…

2012

Challenges: Meeting of the minds

Wins: Liz, FDA telecons/FTF meetings

The Process

2011

Making it up as we go along…

2012

Challenges: Physician payment, CIAs, sharing data

Wins: SharePoint, Scientific Data Disclosure Policy

PRO Consortium Objectives

2011

Broadening our horizons…

2012

Challenges: Keeping in scope

Wins: Communication subcommittee, ePRO subcommittee

Content Validity Stage (New)

2011

Finding a path forward…

2012

Challenges: Project agreements, PRO ownership, mixed methods

Wins: Vendor selection process, expert panels, member participation

Lessons Learned: Asthma Working Group

Linda Nelsen

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Lessons Learned:
Depression Working Group

Steven I. Blum
Forest Research Institute

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Project Initiation/Management

- ***Wins:*** Vendor Selection, Completed Literature/Instrument Reviews, Developed Study Protocol, IRB Approval, Initiated Concept Elicitation Interviews
- ***Challenges:*** Execution of Project Agreements, Agreement on Population/Inclusion/Exclusion Criteria, Project Scope

Expert Panel

- ***Wins:*** Established Expert Panel (*L. Carpenter, J. Fawcett, M. Thase, M. Trivedi*), Held 1st Expert Panel Meeting (WebEx) to Review Study Documents, Scheduled Face-to-Face Item Generation Meeting
- ***Challenges:*** Selection/Recruitment Process, Understanding of PRO/DDT Guidance documents, Scheduling, Engagement

Working Group

- ***Wins:*** Added New Member Firm, Project Management, Completed Scientific Data Disclosure Plan, Submitted Two Research Abstracts
- ***Challenges:*** Representative Turnover, Revisiting Past Decisions, Revision of Diagnostic Criteria (DSM-5), Engagement/Participation of Members

Lessons Learned: Functional Dyspepsia Working Group

Robyn T. Carson
Forest Research Institute

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Scoping Stage Summary Document (SSSD)

- ***Wins:***
  - Superior responsiveness/engagement between the FDA GI Division/SEALD and FD WG to reach consensus on the target patient population
    - Submitted SSSD and received timely feedback from the FDA (< 60 days)
    - Expeditiously granted F2F Type C Meeting
    - Timely resolution
  - SEALD fellow actively involved in FD WG calls to facilitate decision-making on the SSSD revisions
- ***Challenge:*** Defining the FD patient population for qualitative research

Working Group

- ***Wins:***
  - Very engaged representatives from member firms
  - Representatives with different skill sets (eg, PRO, Clinical, Regulatory as needed)
- ***Challenge:*** Scheduling conflicts

Next Steps

- ***Wins:*** RFP developed and issued to coordinating committee for approval in a timely manner
- ***Challenges:***
  - Execution of sponsor contracts and impact on qualitative research timelines
  - Carrying the momentum forward from SSSD stage into qualitative work stage

Lessons Learned: Irritable Bowel Syndrome Working Group

Mollie J. Baird
Ironwood Pharmaceuticals

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Expert Panel Meeting

- ***Wins:***
  - Successfully developed items as a team
    - KOLs, IBS WG member firms, non-member participants, RTI, and C-Path
  - Superior collaboration, communication, and engagement among all team members
  - Meeting preparation and document reviews before the meeting enabled decision making
- ***Challenges:***
  - SEALD presence and feedback in the meeting may have been advantageous

Working Group

- ***Wins:***
  - Very engaged and active representation
  - Non-member participants add value to the discussions
  - FDA and SEALD were actively involved early in the process
- ***Challenges:***
  - Reaching consensus through biweekly teleconferences, which could ultimately compromise the qualitative research timelines
  - Covering all necessary agenda items in biweekly teleconferences
  - Difficulty in coordinating schedules for ad hoc teleconferences

Qualitative Research Stage

- ***Wins:***
  - Member firms were able to watch and listen to patient interviews in real time
  - RTI (vendor) is flexible, collaborative, and knowledgeable in the PRO GI arena
- ***Challenges:***
  - Reaching consensus and making decisions in adherence to the agreed upon timelines
  - Allow more time in between patient interviews to update and obtain feedback from the IBS WG

Lessons Learned: Non-Small Cell Lung Cancer Working Group

Rajiv Mallick, PhD (co-chair)

Daiichi Sankyo

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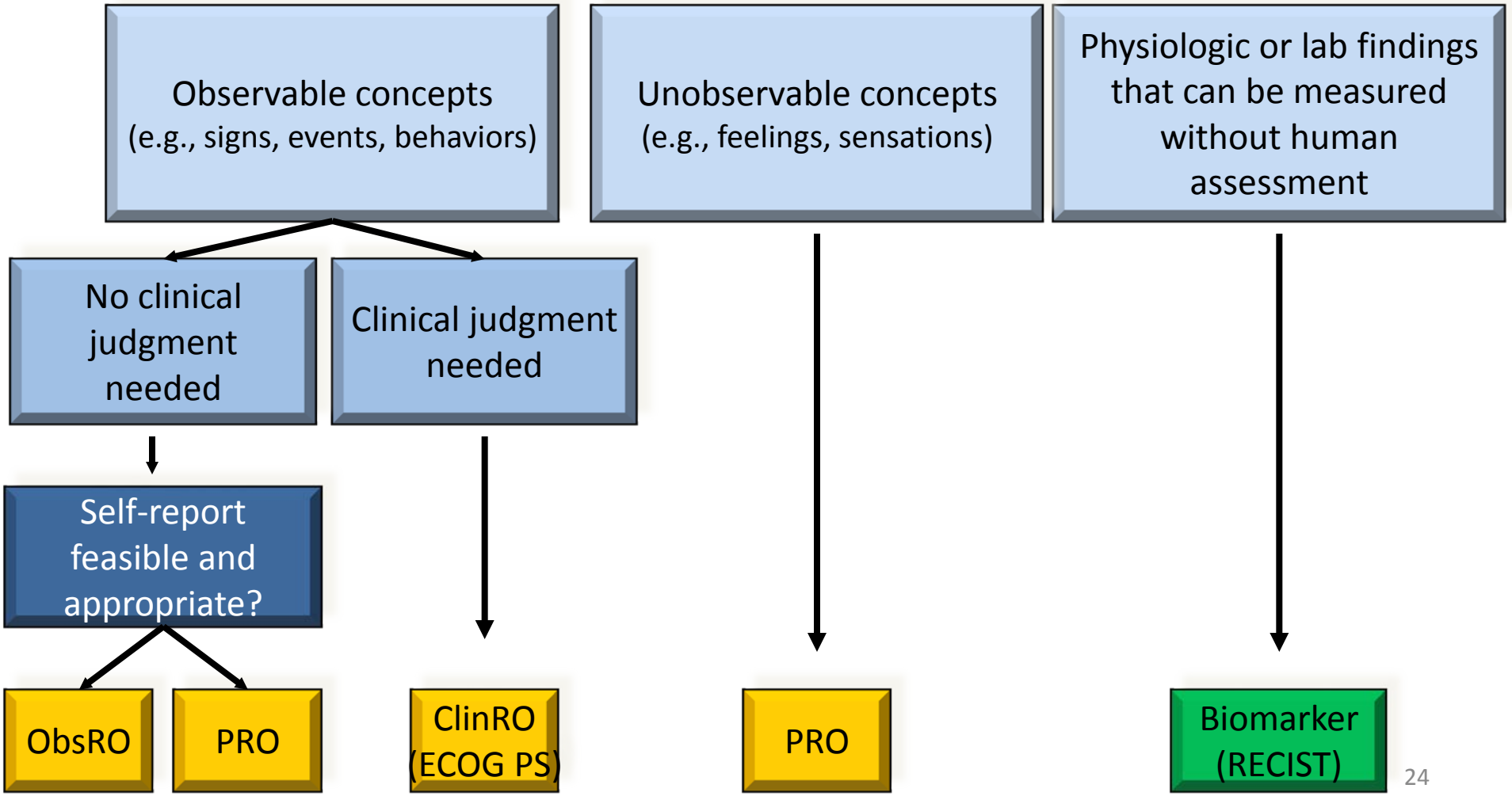
Overview

- Update on progress and issues
- CORE Messages adapted to NSCLC
  - Classification of Endpoint types – Biomarker, Human-Modulated
  - Continuum of Direct vs. More Indirect Patient Benefits
  - Direct Benefits: Concept of measurement (proximal vs. distal to core pathophysiology)
  - Context of Use

Update on Progress

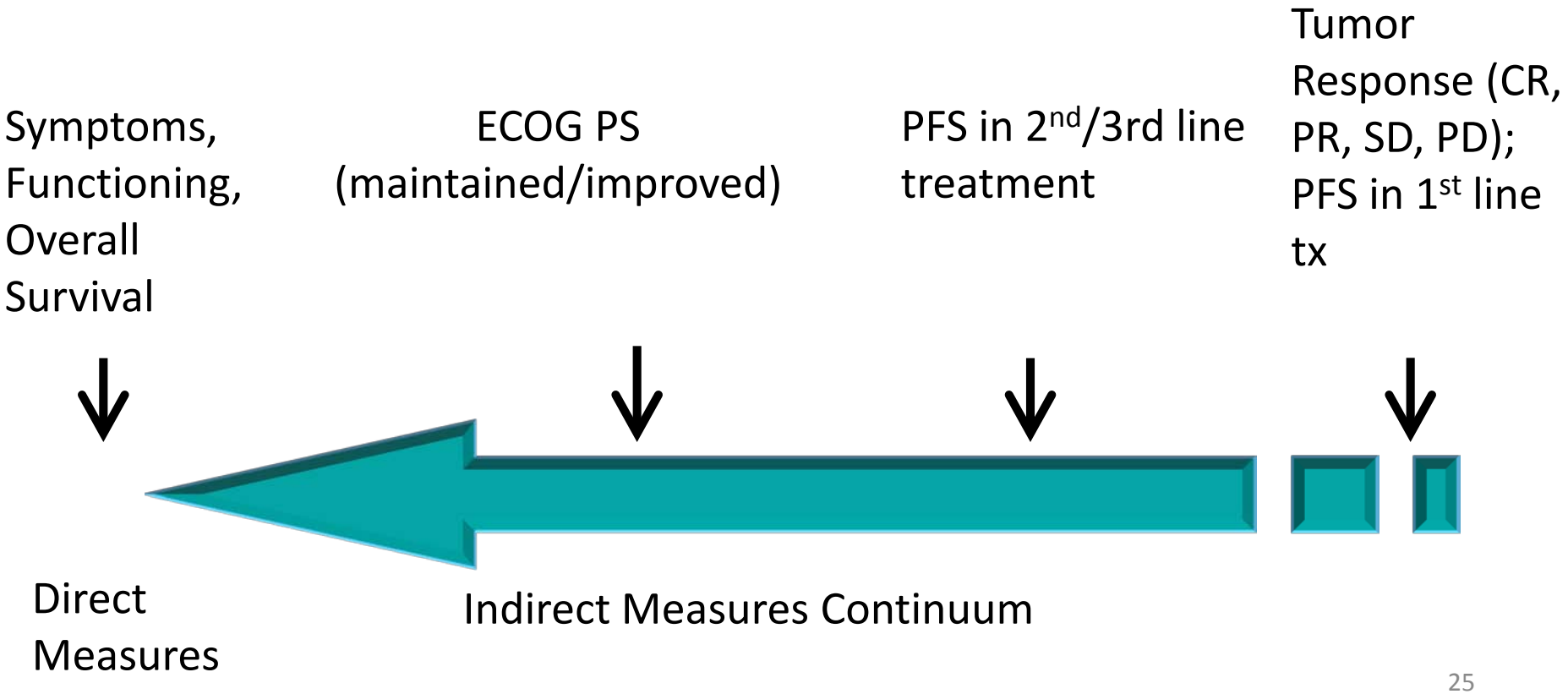
- Scoping Stage, DDT meeting (July 2011)
  - Finalized conceptual framework (living document)
    - Pulmonary vs. non-pulmonary symptoms
    - Symptoms vs. impacts (eg. sleep disturbance, energy)
  - Context of use
    - common target population of registration trials – stage III/IV (exploratory analysis of stage I/II); ECOG PS 0-2
    - Known epidemiology: co-morbid COPD
  - Endpoints
    - Improvement or delayed deterioration in pulmonary symptoms
- Interviewed, finalized vendor (HRA)
- Brief core messages slide deck adapted to NSCLC

Types of Endpoint Assessments to Document Tx Benefit - NSCLC

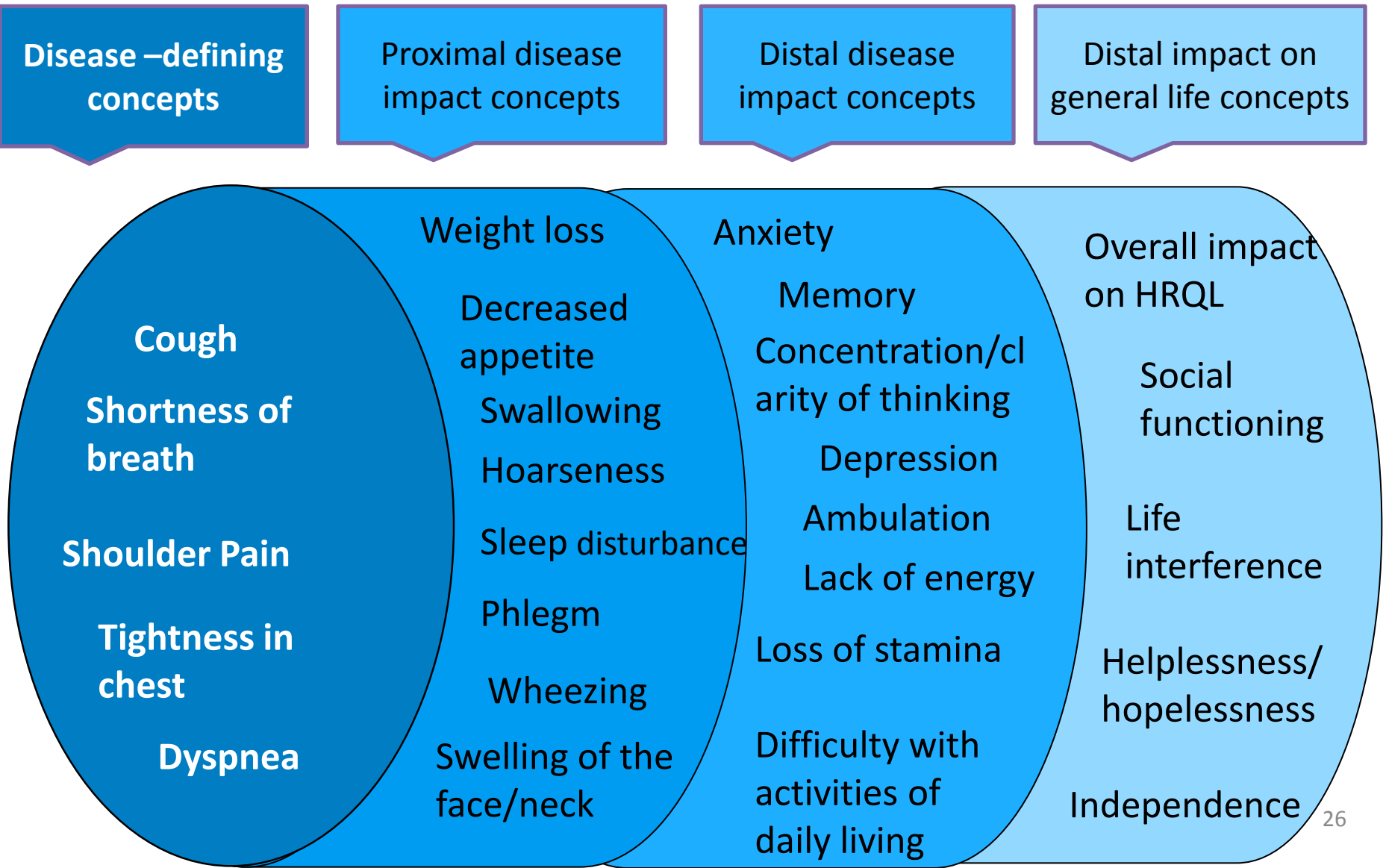


Relationship to Treatment Benefit in NSCLC

- Direct assessment (of tx benefit)
- Indirect assessment (of tx benefit)



Direct Evidence of Tx Benefit: Concepts of Measurement



Context of Use: Endpoint Model

An Endpoint Model displays the role and hierarchy of relevant outcome concepts in clinical trials (i.e., all primary and secondary endpoints)

Endpoint Heirarchy		Concept Endpoints	COA/Biomarker/Survival
Primary	→	Overall Survival	Survival
Secondary with Hierarchy	→	Progression-Free Survival	Biomarker (based on RECIST)
	→	Response	Biomarker (based on RECIST)
	→	Pulmonary symptoms	PRO
Exploratory	→	Non-pulmonary symptoms	PRO

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM205269.pdf

Panel Discussion 5
Lessons Learned: FDA Perspective

Laurie Burke, RPh, MPH

Marc Walton, MD, PhD

Stages of DDT Qualification

Stage	Start	End
Initiation	•DDT tracking # assigned •FDA receives Letter of Intent	•FDA request for initial briefing package
Consultation & Advice	•FDA requests initial briefing package •FDA receives initial briefing package	•FDA request for qualification package
Review	•FDA receives qualification package	•Qualification letter sent & decision posted on FDA website

Initiation Stage

- Request for DDT#
- Letter of Intent
  - Concept of measurement
  - Context of use
    - Disease definition
    - Targeted patient population
    - Study design considerations
    - Targeted claim
- If FDA agrees that a COA is needed, and if FDA determines resources are adequate…
  - FDA agrees to begin the qualification process
  - FDA requests an initial briefing package

Briefing Package

- **Introduction**
  - Concept of measurement
  - Context of Use
  - Overview of current COA development
  - Plan to involve external expertise
- **Summaries**
  - Documentation of content validity
  - Documentation of other measurement properties
  - Interpretation of scores
  - Language translation and cultural adaptation
  - Administration mode
  - Data collection
  - Appendices

Consultation & Advice Stage

- COA developer submits protocols and study summaries (i.e., briefing packages) for FDA input when needed
- Briefing package reviews with discussion and response from SEALD and other relevant disciplines
- When FDA perceives instrument development is complete, FDA will request a Qualification Package

Review Stage

- Qualification Package reviewed by SEALD and relevant disciplines
- FDA communicates review conclusions to submitter
- If qualified, a qualification statement is posted on the FDA website

Lessons Learned—Needs Idenitified

Goal: Quicker response and better advice

- FDA staff is becoming more familiar with DDT program

Initiation Stage

- Need better disease definition and subpopulation identification in advance
- Need more specificity in naming the proposed concept of measurement and context of use

C and A stage

- Need more concise submissions (e.g., study summaries only)
- Earlier submission and advice (generally, sooner is better)

- Review stage
  - FDA needs to provide submission templates
  - FDA needs a review MAPP to clarify the review process

COA Review Status

- Active COA DDTs (26)
  - Initiation Stage: 8
  - Consultation & Advice Stage: 16
    (7 from C-Path PRO Consortium)
  - Review Stage: 2
- Other COA DDTs (10)
  - Declined: 5
  - On Hold: 3
  - Withdrawn: 2

Why then a PRO Consortium?

Two roads diverged in a wood, and I—
I took the one less traveled by,
And that has made all the difference.

Road Not Taken by Robert Frost