An Overview and Discussion with Members of the Friends of Cancer Research Working Group: Comparative Tolerability Trial Design

Ninth Annual Patient-Reported Outcome Consortium Workshop

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FRIENDS of CANCER RESEARCH

Working Group

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Background

- Unmet research need to define tolerability and identify the components of a comparative tolerability trial design

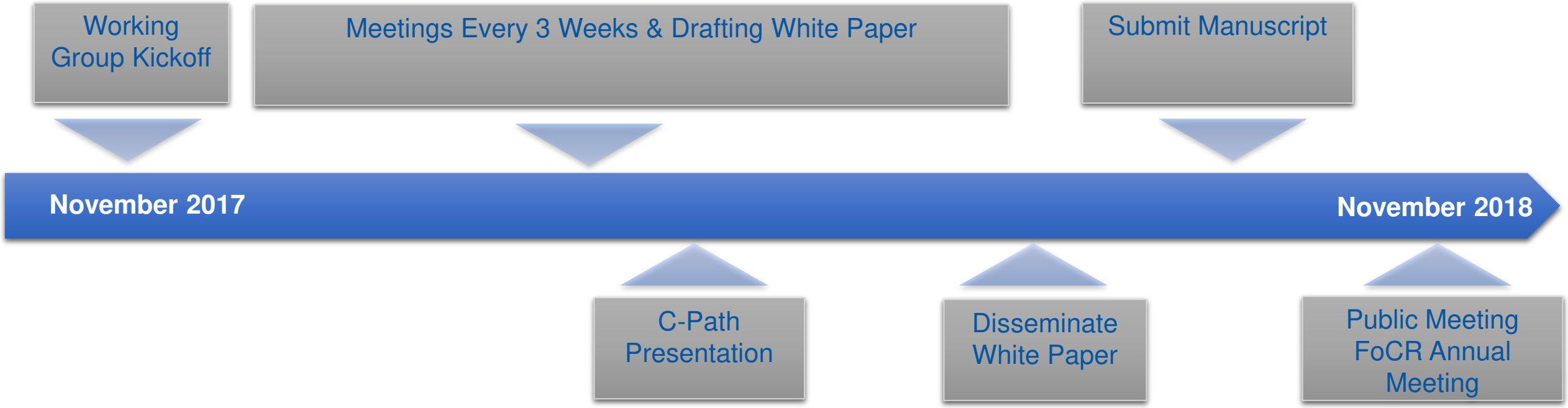
- This is of interest to patients, sponsors, providers, payers, and regulators to provide a pathway for more patient-focused trial designs

- Friends of Cancer Research convened a multi-stakeholder working group to collaboratively develop a working definition of tolerability that better encompasses patient experience; while identifying appropriate endpoints and methods to assist sponsors and regulators in interpreting results for regulatory and clinical decision-making

Working Group Remit and Key Objectives

- Develop a consensus-based definition of tolerability
- Other objectives include the consideration of required data elements (endpoints) and analysis methodologies to characterize tolerability
- Generate a trial design framework with key components and create a case study example for discussion with key stakeholders

Project Timeline



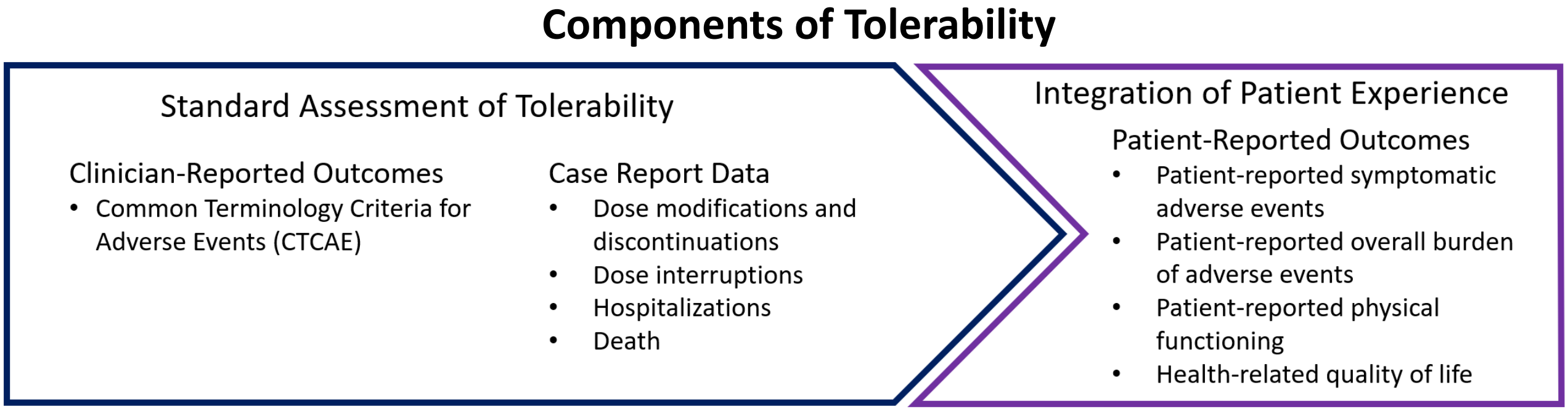
Key Milestones

Date	Deliverable
Spring 2018	Disseminate white paper • Propose new definition for tolerability • Identify core components for assessing tolerability
Summer-Fall 2018	Submit Manuscript • Methods for incorporating tolerability measures into oncology clinical trials • Approaches for collecting, analyzing, weighting the components of tolerability
Fall – Winter 2018	Public meeting/Friends of Cancer Research Annual Meeting • Discuss case study • Discuss how results would be described in the existing labeling framework

Proposed Definition of Tolerability

The tolerability of a medical product is the degree to which symptoms and adverse events associated with the product's administration affect the ability or desire of the patient to adhere to the dose or intensity of therapy. A complete understanding of tolerability should include direct measurement from the patient on how they are feeling and functioning while on treatment.

Working Framework of Data Elements



Why would this be of interest to sponsors?

- Currently, more tolerable regimens than standard of care (SOC) with equivalent or lesser efficacy do not have a clear regulatory path forward to enable their prioritization for commercial development
  - Pathway to bring more patient-relevant treatment regimens to market and increase evidence for patient decision-making on choice of therapy
- The only current design analog is a non-inferiority trial, however that doesn't prioritize the concepts of interest for tolerability assessment and has an efficacy primary endpoint
- The characterization of tolerability has value across multiple cancer trial contexts such as:
  - Informing target dose-finding in early phase
  - Applying the framework to late phase trials to better describe the tolerability of new regimens

Discussion

Alicyn Campbell, MPH Global Head, Patient-Centered Outcomes Research for Oncology Genentech, A member of the Roche group	**Paul Kluetz, MD** Associate Director of Patient Outcomes (Acting) Oncology Center of Excellence U.S. FDA
Lee Jones Patient and Research Advocate	**Mark Stewart, PhD** Senior Science Policy Analyst Friends of Cancer Research

Interested in Learning More?

- Kluetz,P.G. et al., *Informing the Tolerability of Cancer Treatments Using Patient-Reported Outcome Measures: Summary of an FDA and Critical Path Institute Workshop*, Value in Health, 2017. http://dx.doi.org/10.1016/j.jval.2017.09.009

- Pearman, T. et al, *Validity and Usefulness of a Single-Item Measure of Patient-Reported Bother From Side Effects of Cancer Therapy,* Cancer, March 1, 2018.