ONCOLOGY CENTER OF EXCELLENCE

*Project SignifiCanT (Statistics **in Can**cer **T**rials)*

Aim:

To promote collaboration and engagement among different stake holders in design and analysis of cancer clinical trials to advance cancer drug development

Objectives:

- Provide a platform to participate
- Promote non-product specific scientific discussions on design and analysis of cancer clinical trials
- Foster collaboration among regulators, professional organizations, industry, academicians and patients to advance drug development with improved design of cancer clinical trials

Topic for discussion – February 11, 2021

- Statistical considerations in Oncology clinical trials in the COVID-19 era.

The COVID-19 pandemic is transforming oncology clinical trials. The pandemic is affecting many aspects of the clinical trials including the enrollment of patients to clinical trials, mode of interaction between the physician and the patient, and the baseline and outcome assessments. There is a need to discuss overarching guiding principles and points to consider regarding statistical properties in the design, conduct and analyses of oncology clinical trials in the current pandemic and post pandemic era. The aim of these open forum discussions is to understand the points to be considered in future randomized oncology clinical trials. This discussion will be limited to future randomized controlled oncology clinical trials. The assumed objective of the future trial is to demonstrate the benefit of the investigational drug compared to a control (standard of care) in the enrolled patient population. Design of trials, collection and analysis of data, and interpretation of results while maintaining the pre-specified statistical properties will be discussed.

American Statistical Association Biopharmaceutical Section's

Virtual Discussion on: Statistical considerations in oncology clinical trials in the COVID-19 era

Host: Statistical Methods in Oncology Scientific Working Group and LUNGevity Foundation,

in coordination with the Oncology Center of Excellence, US Food and Drug Administration

February 11, 2021

8 am – 10 am EST (New York)

Agenda

Meeting Moderators:

Dr. Elizabeth Barksdale, LUNGevity Foundation

Dr. Qi Jiang, Seagen, Co-chair of ASA BIOP Statistical Methods in Oncology Scientific Working Group

Dr. Olga Marchenko, Bayer, Co-chair of ASA BIOP Statistical Methods in Oncology Scientific Working Group

Dr. Rajeshwari Sridhara, Oncology Center of Excellence, FDA

1. **8 am – 8:10 am: Welcome and Introduction**
    - Dr. Olga Marchenko, Bayer
    - Dr. Richard Pazdur and Dr. Rajeshwari Sridhara, Oncology Center of Excellence, FDA

2. **8:10 am – 9:00 am: Presentations**

    Academia
    - Dr. Sumithra Mandrekar, Mayo Clinic

    Industry
    - Dr. Daniel Li, BMS, on behalf of industry statisticians (BWG)
    - Mr. Evgeny Degtyarev, Novartis & Dr. Kaspar Rufibach, Roche, on behalf of the oncology estimand working group

    Regulatory
    - Dr. Erik Bloomquist, FDA

3. **9:00 am – 9:50 am: Panel Discussion**
    - Panelists: Dr. Richard Pazdur (FDA), Members from International Regulatory Agencies, Prof. Martin Posch (Medical University of Vienna), Dr. Boris Freidlin (NIH/NCI), Dr. Richard Simon (Simon Consulting), Dr. Bohdana Ratitch (Bayer), Speakers
    - Audience participation

4. **9:50 am – 10:00 am: Concluding remarks**
    - Dr. Qi Jiang, Seagen
    - Dr. Elizabeth Barksdale, LUNGevity Foundation
    - Dr. Richard Pazdur and Dr. Rajeshwari Sridhara, Oncology Center of Excellence, FDA

Meeting minutes: Dr. Hong Tian (Janssen)

Presenters Biographies

In order of appearance

Sumithra J. Mandrekar, Ph.D. is Professor of Biostatistics and Oncology at the Mayo Clinic in Rochester MN. She is the Group Statistician for the Alliance for Clinical Trials in the Oncology Statistics and Data Management Center. Scientifically, she has collaborated on the design and analysis of several Phase I, Phase II, and Phase III clinical trials and research projects in the areas of lung cancer and Leukemia.

Dr. Mandrekar serves as the lead statistician for the ongoing ~8300 patient national screening trial in adjuvant lung cancer, A151216 (ALCHEMIST), which is part of the NCI precision medicine initiative. She is actively involved in methodological research work related to the design of clinical studies in areas of adaptive dose-finding trials, initial and definitive biomarker validation trials, identification of alternative Phase II cancer clinical trial endpoints, and research addressing improvements in clinical trial conduct.

Dr. Mandrekar has co-authored over 150 original papers; several book chapters and editorials; and has given numerous lectures, invited presentations and workshops on these topics. She is currently a member of the NCI clinical trials and translational research advisory committee (CTAC), and serves on the NCI thoracic malignancies steering committee, and the biostatistics editor of the Journal of Thoracic Oncology. Dr. Mandrekar is active in many statistical and clinical societies, including serving as the president of the Society for Clinical Trials in 2018-2019.

Presenters Biographies

In order of appearance

Daniel Li, PhD, VP and Head of Cell Therapy Biostatistics at BMS. He has over 15 years experiences in design and analysis of clinical trials in pharmaceutical industry. He received his Ph.D. and M.Sc. in Statistics from University of Manitoba. His research interests are Bayesian dose-finding trials, adaptive trial designs and in measurement errors.

He authored/co-authored over 30 papers published in peer-reviewed statistical/clinical journals. Dr Li served as the board director for International Chinese Statistical Association (ICSA), and he is an active member of American Statistical Association (ASA) and the American Society of Clinical Oncology (ASCO).

Evgeny Degtyarev is leading a team of quantitative scientists on a hematology program at Novartis. Since joining Novartis in 2013 he supported several oncology programs with targeted and immunotherapies in different stages of development. He has co-founded and co-leads the industry working group “Estimands in oncology” since 2018.

Kaspar Rufibach is an Expert Statistical Scientist in Roche's Methods, Collaboration, and Outreach group and located in Basel. He does methodological research, provides consulting to Roche statisticians and broader project teams, gives biostatistics trainings for statisticians and non-statisticians in- and externally, mentors students, and interacts with external partners in industry, regulatory agencies, and the academic community in various working groups and collaborations. He has co-founded and co-leads the European special interest group “Estimands in oncology” (sponsored by PSI and EFSPI, which also has the status as an ASA scientific working group, a subsection of the ASA biopharmaceutical section) that currently has 55 members representing 28 companies and several Health Authorities and works on various

Presenters Biographies

In order of appearance

topics around estimands in oncology. Kaspar's research interests are methods to optimize study designs, advanced survival analysis, probability of success, estimands and causal inference, estimation of treatment effects in subgroups, and general nonparametric statistics. Before joining Roche, Kaspar received training and worked as a statistician at the Universities of Bern, Stanford, and Zurich. More on the oncology estimand WG: http://www.oncoestimand.org More on Kaspar: http://www.kasparrufibach.ch

Dr. Erik Bloomquist is a mathematical statistician and team leader in the Division of Biostatistics 5, Office of Biostatistics, Office of Translational Sciences, Center for Drug Evaluation and Research (CDER). He has over 10 years of experience at FDA working in the Center for Devices and Radiological Health (CDRH) and CDER. His research interests include: prediction and forecasting models for survival analysis, auditing methods for blinded independent central review, and methods to derive balanced cohorts from multi-cohort external controls.