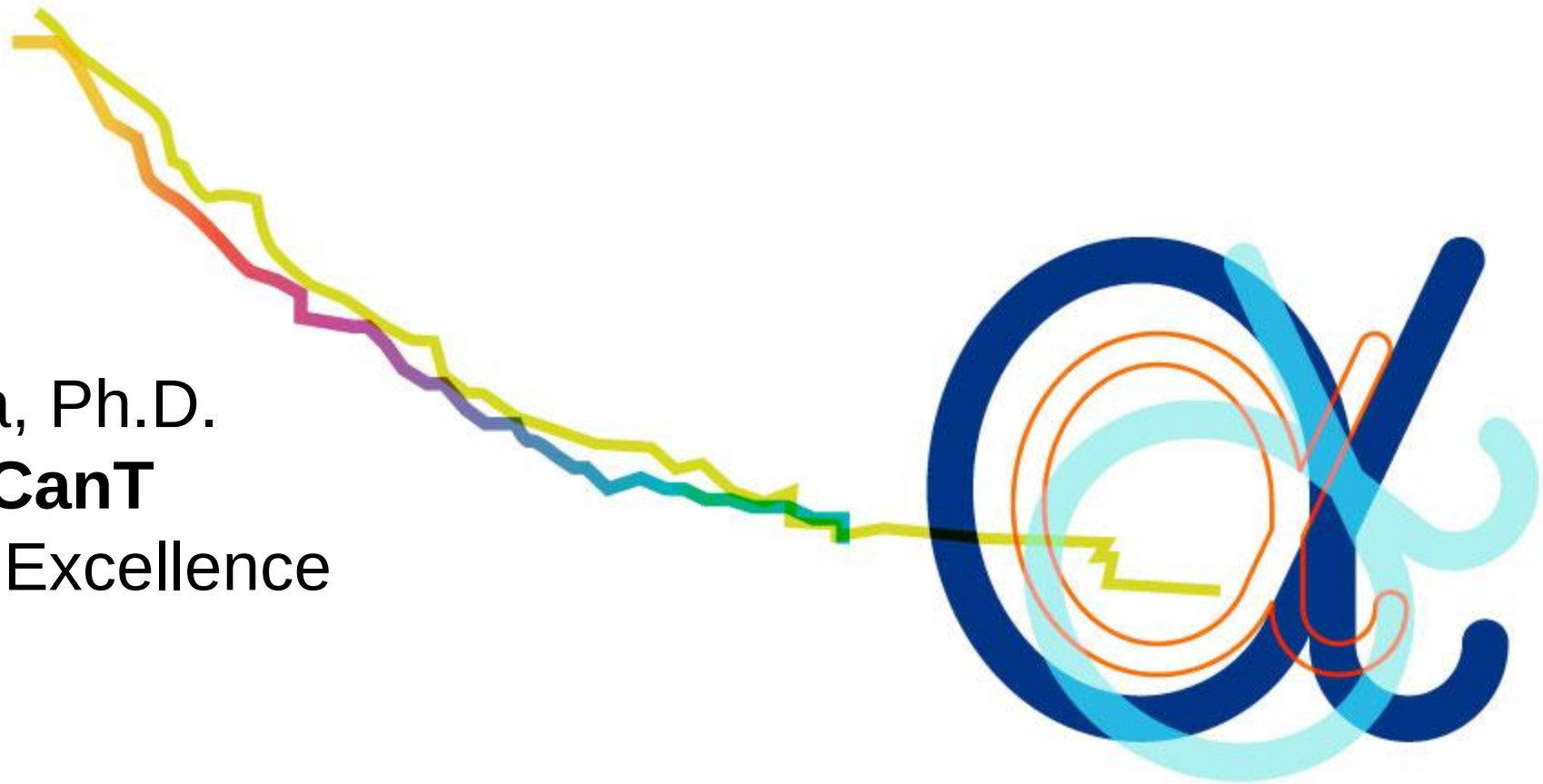
Project **S**igni**fiCanT**

Rajeshwari Sridhara, Ph.D.
Lead Project **S**igni**fiCanT**
Oncology Center of Excellence
US FDA



7th EFSPI Regulatory Statistics Workshop
Sept 15, 2022, Basel

Outline

- Oncology Center of Excellence, FDA
- Project Initiatives in OCE
- Project **S**igni**fiCanT**
- Concluding Remarks

Oncology Center of Excellence

Oncology Center of Excellence | FDA

Vision

We seek to create a unified and collaborative scientific environment to advance the development and regulation of oncology products for patients with cancer.

Mission

The mission of OCE is to achieve patient-centered regulatory decision-making through innovation and collaboration.

Oncology Center of Excellence

- OCE was authorized by the 21st Century Cures Act of 2016 and was established in January 2017
- In addition to the review of medical products for oncologic and hematologic malignancies, OCE leads a variety of research and educational outreach projects and programs
- The theme of all project initiatives is collaboration and innovation
  - E.g.: Project Orbis, Project Optimus, Project Equity, Project Silver, Project Socrates, Project SignifiCanT, etc.

Project **S**igni**CanT** (**S**tatistics in **Can**cer **T**rials) Oncology Center of Excellence, USFDA

Project Significant: Statistics in Cancer Trials | FDA

Aim:

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

Team: Dr. Richard Pazdur (Director, OCE), Dr. Marc Theoret (Deputy Director, OCE) and Dr. Rajeshwari Sridhara (Statistical Consultant, OCE)
Project Manger: Ms. Joan F Todd

Project **S**igni**fi****CanT** (**S**tatistics in **Can**cer **T**rials)
Oncology Center of Excellence, USFDA

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

Collaborators/Discussion Hosts

- American Statistical Association Biopharmaceutical Section
  - Pharmaceutical Statisticians/Clinical Trialists, Academicians, Consultants, etc.
- LUNGevity Foundation
  - Patients, Clinical Investigators, Patient Advocacy Groups, etc.
- International Regulatory Bodies
  - FDA, EMA, HC, PMDA, TGA, MHRA, SMC, ANVISA, Singapore, Israel

Discussion Format and Topics

- Virtual discussions by invitation hosted by ASA-BIOP; duration 2 hours
- 100 - 120 participants including participation by senior OCE management
- Brief introduction to the topic followed by 2-3 short presentations followed by panel discussion
- Panel includes international regulators, industry representatives, academicians, clinicians, patients/patient advocates and representatives from other disciplines depending on the topic of discussion
- Variety of topics on critical statistical issues involving collaboration from all stakeholders
- Chairs for the discussion meetings: Drs Olga Marchenko (Bayer) and Qi Jiang (Seagen) from ASA BIOP working group, Dr. Elizabeth Barksdale from LUNGevity Foundation, and Dr. Rajeshwari Sridhara from OCE

Open Forum Topics Discussed

- Type I error Considerations in Master Protocols with Common Control in Oncology Clinical Trials
- Use of Non-concurrent Common Control for Treatment Comparisons in Master Protocols
- Statistical Considerations in Oncology Clinical Trials in the COVID-19 Era – Part I and Part 2
- Designing Dose-optimization Studies in Cancer Drug Development – Part 1,2 and 3
- Evaluation of Treatment Effect in Underrepresented Population in Oncology Clinical Trials – Part I and Part 2
- Statistical Considerations in Pediatric Cancer Trials – Part 1 and Part 2
- Summarizing Treatment Effect for Time-to-event Endpoints in Cancer Clinical Trials in the Presence of Non-proportional Hazards – Part 1 and Part 2

Open Forum Topics Discussed

- Cancer Clinical Trial Design Considerations when Accepting Foreign Data from a Single Country
- Cancer Clinical Trial Design Considerations in Evaluating Treatment Effect in Marker Negative Population
- Impact on Type I error with Unplanned Analyses in Cancer Clinical Trials
- Statistical Considerations in the Evaluation and Interpretation of Interim Overall Survival Results in Patients with Chronic Diseases from Randomized Cancer Clinical Trials
- Considerations for Data Monitoring Committee and Regulator Direct Interactions in Ongoing Randomized Cancer Clinical Trials
- Considerations in the Evaluation of Progression-fee Survival with Informative Censoring in Cancer Clinical Trials

19 Discussions held to date since initiating in October 2020

Publications

- Summary of American Statistical Association Biopharmaceutical Section's Virtual Discussion with Regulators on Type I Error Considerations in Master Protocols with Common Control in Oncology Clinical Trials; https://higherlogicdownload.s3.amazonaws.com/AMSTAT/fa4dd52c-8429-41d0-abdf-0011047bfa19/UploadedImages/BIOP%20Report/BIOP_fall2020_Final_Updated.pdf
- Use of Non-concurrent Common Control for Treatment Comparisons in Master Protocols; https://higherlogicdownload.s3.amazonaws.com/AMSTAT/fa4dd52c-8429-41d0-abdf-0011047bfa19/UploadedImages/BIOP%20Report/BIOP_winter2021_final.pdf
- Sridhara R, Marchenko O, Jiang Q, et.al. Type I Error Considerations in Master Protocols With Common Control in Oncology Trials: Report of an American Statistical Association Biopharmaceutical Section Open Forum Discussion; Statistics in Biopharmaceutical Research 2021 https://doi.org/10.1080/19466315.2021.1906743
- Sridhara R, Marchenko O, Jiang q, et.al. Use of Nonconcurrent Common Control in Master Protocols in Oncology Trials: Report of an American Statistical Association Biopharmaceutical Section Open Forum Discussion; Statistics in Biopharmaceutical Research 2021; https://doi.org/10.1080/19466315.2021.1938204

Publications

- Summary of American Statistical Association Biopharmaceutical Section's Virtual Discussions with Regulators on Statistical Considerations in Oncology Trials in the COVID-19 Era; https://higherlogicdownload.s3.amazonaws.com/AMSTAT/fa4dd52c-8429-41d0-abdf-0011047bfa19/UploadedImages/BIOP%20Report/BioPharmSummer2021_FINAL.pdf
- Summary of ASA Virtual Discussion with Regulators on Designing Dose-Optimization Studies in Cancer Drug Development; https://higherlogicdownload.s3.amazonaws.com/AMSTAT/fa4dd52c-8429-41d0-abdf-0011047bfa19/UploadedImages/BIOP%20Report/BioPharmSummer2021_FINAL.pdf
- Summary of American Statistical Association Biopharmaceutical Section's Virtual Discussions with Regulators on Evaluation of Treatment Effect in Underrepresented Population in Oncology Clinical Trials; https://higherlogicdownload.s3.amazonaws.com/AMSTAT/fa4dd52c-8429-41d0-abdf-0011047bfa19/UploadedImages/BIOP%20Report/BioPharmSummer2021_FINAL.pdf
- Summary of ASA Virtual Discussion with Regulators on Statistical Considerations in Clinical Trials for Rare Pediatric Cancers; Biopharmaceutical Report, 2022, Vol 29, No 1, pp 30-32.
- Cancer Clinical Trials Beyond Pandemic: Report of an American Statistical Association Biopharmaceutical Section Open Forum Discussion. Statistics in Biopharmaceutical Research, 2022, July 25 (online).
- Summary of ASA BIOP Section's Virtual Discussion with Regulators on Time-toevent Endpoints in Cancer Trials in the Presence of Non-Proportional Hazards; Biopharmaceutical Report, 2022 Vol 29 No 2, pp 42-45

Concluding Remarks

- Goal of all stakeholders is to bring safe and effective drugs to cancer patients
- Out of the box thinking, innovation and COLLABORATION are key to solving difficult problems
- All recommendations/decisions are based on data
- Statisticians are in a unique position to bring stakeholders from all relevant disciplines to the table. We can learn from our past experiences, and do better in future cancer trials with more thoughtful design, conduct and analyses of data
- Project **S**igni**fiCanT** is one such successful initiative to foster collaborations