

Strategies to Improve Cardiovascular Phenotyping in Cancer Clinical Trials

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Phenotypic Characterization differs between Oncology and Cardiology

- Oncology
 - Characterize the cancer (**histology**)
 - “Tissue” Phenotype (histology, genetic and other markers)
 - Determine Cancer Treatment based upon the tissue phenotype and stage of disease

- Cardiology
 - Characterize the physiology of the patient’s cardiovascular system (**function**)
 - Cardiovascular Phenotype (imaging, markers, EKG, etc)

Challenges with Cardiovascular Phenotype for Cancer Patients

- Assessing cancer patients for non-cancer conditions prior to cancer therapy
 - Patients typically need treatment quickly
 - Trial eligibility usually excludes co-morbidities
- Balancing the data collection for agents that may not have the promised efficacy
 - Patients may receive a few cycles of therapy in phase 1 or 2 trials
- Adverse event not occur immediately
 - Recognize effects later in drug development

Cardiovascular Phenotype varies by Therapeutic Intent

- Advanced Disease

- Patients need ongoing treatment (months to years)
- The CV AE could limit delivery of treatment
- Manage the patient through the toxicity to maintain ongoing treatment

- Early Disease

- Patients receive short course of treatment to prevent recurrence
- May never get recurrence, but willing to take the risk of the drug to reduce the risk of recurrence
- Typically, the CV AE does not limit delivery of the agent, but may be a long term or late effect.

Adverse Event Reporting versus Monitoring

- Reporting an Adverse Event
 - Report occurrence (expected & unexpected)
 - Clinical assessment, not uniform
 - Manage patient to reduce functional impairment from the AE

- Monitoring an Event
 - Follow trajectory of event over time
 - Prospectively identify standard assessment across patients and over the course of the trial
 - Protocol Specific Instructions

CTCAE Cardiac Events

- Revisions for some cardiac events still under internal discussion
- Need consistent severity grading across all events
 - Language for some cardiac Grade 3 events may specify hospitalization
- Heart Failure vs Left Ventricular Dysfunction vs drop in Left Ventricular Ejection Fraction
 - Events Different
 - Clarify for ease of reporting by oncology sites

Session #4

- Pediatric Survivors (Steven Lipshultz, MD)
 - Monitoring and prevention of CV toxicities
- Cardiovascular Phenotype in Cancer Cooperative Group Trials (Bonnie Ky, MD)
- Designing and Implementing CV safety registries
 - (Dan Lenihan, MD)
- Regulatory path (Suparna Wedam, MD)



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