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)