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Guiding Principles for Efficient Data Collection

20 Years of CV Outcomes Trials

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Does the Few Page CRF Even Exist?

Cardiovascular Outcomes Trial Profile

- Phase 3-4 drug trials
- 5000- 20,000 patients in 15-50 countries
- Acute (ADHF, AMI/ACS, PCI) and Chronic (lipids, primary, secondary prevention post AMI/ACS)
- Intent to treat analysis with DSMB; endpoints adjudicated
- Typically double blinded
- No run in phase
- Monitoring- infrequent on-site visits, RBM
- AE Reporting-typically negotiated with regulatory

DCRI Guiding Principles

1. Have we enrolled the right participants according to the protocol with adequate consent?
2. Did participants receive the assigned treatment and did they stay on the treatment?
3. Was there complete ascertainment of primary and secondary efficacy data?
4. Was there complete ascertainment of primary and secondary safety data?
5. Were there any *major* GCP related issues?

Streamlining By Section

- Past Medical History
- Physical Exam, Labs/Vital Signs
- Post Randomization Events
- Con Meds
- SAEs

PMH- Focus on Risk Factors/Predictors of Risk

5.*	Hypertension	○ Yes Currently medically treate ○ Yes ○ No ○ No
6.*	Cigarette smoking	○ Currently smoking ○ Prior history of smoking (N Year most recently quit ○ Never smoked
7.*	Angina pectoris	○ Yes Current CCS class ○ I ○ II ○ III ○ IV ○ No
8.*	Coronary stenosis >70 % documented in at least 1 major epicardial coronary artery	○ Yes ○ No

Labs, Physical Exam and Vital Signs

- Part of the Primary Endpoint definition: record all
- NOT Part of the Primary Endpoint: collect either nadir or peak, closest to critical event or not at all
- Baseline PE rarely if ever collected

Post Randomization Events

2.*	Death	○ Yes ○ No
3.*	Myocardial infarction	○ Yes ○ No
4.*	Stroke	○ Yes ○ No
5.*	TIA	○ Yes ○ No
6.*	Unstable angina / recurrent ischemia or any chest pain that led to intervention / hospitalization	○ Yes ○ No

Concomitant Medications

- Classes of Meds with check boxes for time periods (on admission, at enrollment, at discharge)
- Dosing Details limited to (similar) Medications of Interest (ie antiplatelets, diabetes Rx, lipid Rx)
- Non- collection of drugs given during procedures- CABG, PCI
- “Snapshots” of Meds during long-term follow-up
- SAEs- all meds, all details pertinent
- All meds, all details (i.e route, dose, start/stop)

Summary

- **Develop Guiding Principles to drive data collection**
  - Focus on primary safety and efficacy definitions
- **Recognize limitations for answering "All Questions"**
- **Utilize Yes/No check boxes- PMH, Post Randomization Events, Endpoints**
- **Utilize lists for expected events- ie. Arrhythmias, hypoxia**
- **Negotiate with Regulatory Authorities on AE reporting**

Over the Ages -Size of CRF

- **1990- GUSTO, thrombolytic therapy in AMI**
  - 3 page baseline + 30 day postcard
- **1995- PURSUIT, glycoprotein IIbIIIa Inhibitor in PCI**
  - 10 page baseline + 1 page 30 day
- **2008-ROCKET AF, oral anti-Xa inhibitor in atrial fib**
  - 20 page baseline + 7 page monthly + event pages
- **2011-dalOutcomes 2, CETP inhibitor in stable CAD**
  - 7 page baseline + 7 page q 6 mos + event pages
- **2012- Secondary Prevention post ACS, injectable, PCSK9**
  - 20 page baseline + 10 page q 3 mos + event pages

THANK YOU

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