NSVT without QT Prolongation
Is it Relevant in Clinical Development?
Role of More Intensive Monitoring?

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NSVT w/o QT Prolongation

- Monomorphic or polymorphic
- Potential mechanisms relevant to drug development
  - Ischemia
  - Thrombosis
  - Fibrosis
  - Myocarditis
  - Pericarditis
  - Catacholaminergic effects
Drug A (metabolic blocker)

- Approved drug for fatal disease
- Animal studies – cardiac failure, fibrosis, hemorrhage, TnT elevations
- V-tach reported in clinical trials (? Long QT)
- Labeled warnings
  - Cardiac failure (decreased LVEF)
  - Myocardial infarction-DVT-PE (thrombotic process)
  - Restrictive cardiomyopathy (fibrotic process)
  - Death due to cardiac arrest within one day of administration
Drug B (metabolic blocker)

- Approved for fatal disease
- Acute STT-wave change c/w ischemia
- Presumed vasospasm
- First exposure predominance
- Pulseless VT and primary VF

Sympathomimetics

• Drug C
  – Labeled warning for ventricular arrhythmias
  – Used for ventricular arrhythmia induction at electrophysiology study

• Ephedra-induced ventricular tachycardia
Drug D (metabolic blocker)

- First in class for potentially fatal disease
- No QT prolongation in animals/human, but elevated cardiac troponin I seen in several animals of two species
- One animal had 4 beat run of NSVT
- FIH and SAD study in humans no issues
- First human MAD study, two DR/TE AEs
  - Transient low-grade cTnI elevation
  - NSVT per the following EGC
Drug D: Should Development Path Change?