

# Defining unmet needs, clinical study barriers, targets for drug and device therapy for shock: FDA view

Ileana L. Piña, MD, MPH

Professor of Medicine

Albert Einstein College of Medicine

Senior Staff Fellow and Medical Reviewer, FDA, CDRH

September 7, 2018

# Scope of this Commentary

- Not limited to CDRH
- Cardiogenic shock is a physiologic state in which inadequate tissue perfusion results from cardiac dysfunction, most commonly following acute MI., decreased C.O. and evidence of tissue hypoxia in the presence of adequate intravascular volume.
- Hemodynamic criteria: sustained hypotension (systolic blood pressure <90 mm Hg for at least 30 minutes) and a reduced C.I.<2.2 L/min/m<sup>2</sup> in the presence of an high PCP >15 mm Hg.

# Cardiogenic Shock: Etiologies

- Failure to wean from CPB
- Cardiogenic shock (acute MI)
- Acute decompensation of chronic HF
- Pending recovery
  - Post-partum
  - Myocarditis
- First presentation of HF in an acute setting

# Cardiogenic shock : The issues

- What the sponsor proposes for the label and intended use
  - Maintenance of perfusion to vital organs
    - BP is the surrogate for perfusion
    - Lactic acid
    - Renal function
  - e.g., Extracorporeal Circulatory support with an external control unit
  - Partial or total support
- Need to clearly define populations
  - Higher mortality in >75 y.o.
  - Restrict to <75?
  - Source of cardiogenic shock: Myocardial infarction/profound ischemic vs. others
- Who are the patients: Are there preliminary or pilot data already?
- Length of use, depends on the intended use

# Short vs. very short intended use

- 3 potential outcomes to CS
  - Death
  - Maintain patient for revascularization
  - Recovery
  - Persisting to require bridge
  - Maintain patient for decision to longer duration support or futility
- Define duration of support
- Maintain blood pressure, improve organ perfusion
  - Renal function
  - Lactic acid
  - Support to allow revascularization

# Intended Use

- Very Short (temporary) support e.g., <6 hours
- Short term ventricular support e.g., 2-6 days
  - May be a bridge to a decision
- Note: Short term may need mortality
  - Alive without stroke
  - If stroke, NIH scale
  - Endpoint may be short as well, how short depends on the indication of use
    - Hours if for support in high risk PCI to revascularize in CS
    - Failure to wean off CPB—hours to days to recovery or decision
    - Placement within 48 hours not responsive to dilators or pressors

# Intermediate Time

- Pending recovery (?)
  - If recovery is possible, what is the timeline
    - Published literature
- Bridge to transplant

# “Longer” Term Endpoints

- Timing of endpoint related to length of time on a drug or device
  - e.g. Alive in 30 days without a stroke
  - Alive out of hospital
  - Alive to transplant or long term MCS
  - Repeat hospitalizations
  - Incidence of HF
  - Health status at 30 days
  - Functional capacity (NYHA, 6 min walk, ET)
  - Preservation of organ function

Thank you