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

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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/m² 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