DEBATE: Not So: Controversy Lingers: We Do Need A RCT For Acute Uncomplicated TBADs: How Could Such A Trial Be Structured And Financed?!

Firas F Mussa, MD

Disclosure

- A friend
- He was behind starting the effort
- Mega-INSTEAD→INTACT-AD
- So, he definitely agrees with me → no debate

INSTEAD-XL

- Primary endpoint was mortality at 2 years
- Effect size calculated to be 80% (23%→6%)
- Clearly underpowered and small in scale and impact
  - TEVAR should be delayed >2 weeks
  - Aortic remodeling (curse)
  - Landmark analysis
  - Over 1000 remaining questions since!

Current TEVAR Push

- Anatomical and observational data
- Existing practice paradigms-VQI (device safety)
- Strong conflict/bias in favor of TEVAR (PCI over CABG, PTA over leg bypass, CAS over CEA)
- Well-powered, randomized trials show the “conventional wisdom” to be incorrect, and ultimately changed practice

Last weekend @ AHA...

- ISCHEMIA: 5179. >400 sites, $100M, SIHD with mod-severe stenosis on CCTA
- Asymptomatic
- Symptomatic
- QoL was improved at 1 year with INV

Made History!!!!

- 1000 patients
- 50 sites
- MAC-free survival: major open repair
- 48 hours-90 days
- $10M
- Reviewed by CLTR in 6/19
  - Significance
  - Innovation
  - Investigators
  - Approach
  - Environment

- Unenrollmited Type B Aortic Dissection: Made INTACT-AD and Inspiring others
**June 2020**

- **Primary endpoint:** All-Cause Mortality @ 5 yr
- **Sample Size:** 30% effect size with 30% event rate, 85% power = 720, 90% power = 840
- **Select secondary endpoints:** VQI-Medicare Link*
- **Partner with Gen-TAC Alliance
- **Partner with PCORI: (Engaging Patients with Type B Aortic Dissections as Partners in Patient-Centered Outcomes Research)**

---

**Ancillary Studies**

- **Imaging:** The aim of prospectively collecting imaging data is two folds. First: to study the natural history of uncomplicated TBAD treated with TEVAR or MT alone over time. Second: identify the radiologic characteristics that are related to later aortic expansion, development of acute complications (rupture and malperfusion syndrome) or death
- **Cost and Cost-Effectiveness (HEOR):** Treatment-associated costs (in- and out-patient); Incremental CE measured in dollars per quality adjusted life years (QALY)

---

**My thoughts…**

**Generalizability and Implications of Potential Trial Results**

Regardless of the results of INTAC-AD, the outcome of this 1000 patient trial will provide robust evidence to inform guideline recommendations that are currently based on outdated and weak evidence for uTBAD. This should have substantial impact on practice. Precise interpretation will depend not only on the primary endpoint comparison but also its components and other secondary endpoints, especially quality of life and cost effectiveness.

---

**10/12/18: Email to 100 investigators: 90 replied in 48h**

- **DO YOU THINK THERE IS CLINICAL EQUIPOISE IN THE MANAGEMENT OF UNCOMPPLICATED TBAD? 90 YES**
- **DO YOU CURRENTLY STENT ALL COMERS? BASED ON IMAGING? ONLY IF THEY DEVELOP COMPLICATIONS?**

We received 95 replies within 48 hours: 67 vascular surgeons, 23 cardiac surgeons and 5 cardiologists
9/6/2019: 113 emails

- 1. DO YOU THINK A PROPERLY POWERED TRIAL ALONG WITH FUNDED REGISTRY IS NEEDED/JUSTIFIED/ETHICAL?
- 2. DO YOU THINK THAT THE CURRENT SVS-VQI POST MARKET STUDIES AND/OR IRAD IS ENOUGH TO STUDY THE NATURAL HISTORY OF UTBAD WHO ARE TREATED WITH TEVAR OR OMT?

We received 93 replies within 36 hours: 66 vascular surgeons, 21 cardiac surgeons and 6 cardiologists

• **Significance**
  - Role of registry and industry trials
  - Technology development during the trial
  - Primary endpoint-open repair
  - Enrollment, contingency plans

• **Investigators**
  - NO NIH trial experience of the PIs
  - COI of investigators
  - PMP-assign a PM
  - 4 PIs
• **Innovation**
  - Timing of randomization (48-72 hours)
  - Definition of uncomplicated
  - Claims data

• **Approach**
  - Outreach to FDA, industry and patients
  - Standardization across sites of training, screening, data collection, reporting and site coordinators
  - Pharmacovigilance
  - Justify the event rate
• **Environment**
  - Site details
  - Enrollment and timeline