

**International Study Of Comparative
Health Effectiveness With Medical And
Invasive Approaches (ISCHEMIA):
*Primary Report of Clinical Outcomes***

Discussion

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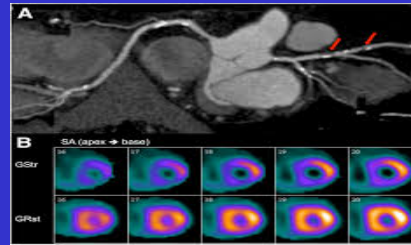
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Relevant Relationships with Industry (RWI): None

AHA 2019

ISCHEMIA Trial Analysis



Conservative

GDMT

Invasive

- **Question** - important, new
- **Design** - bias, relevance, fidelity
- **Sample Size** - adequate
- **Endpoints** - justified
- **Conclusions** - supported by data
- **Applicability** - influence clinical practice

ISCHEMIA Trial Analysis

- **Question**
 - important, conflicting data, equipoise
- **Design**
 - Randomized, multicenter, multi-country, superiority, comparative effectiveness, **quality of life**
 - Investigators unblinded, CEC blinded, no sham control
 - Absence of coronary angiography prior to entry mitigates potential selection bias against higher risk anatomy which previously may have diminished effect of revascularization

ISCHEMIA Trial Analysis

- ***Design***

- Pre-specified Bayesian analysis to directly estimate probability of a difference in the treatment strategies
- Relevant population studied – 87% population with moderate or severe ischemia
- Fidelity – implemented multiple methods from trial inception to mitigate bias in the ascertainment of events

ISCHEMIA Trial Analysis

- **Sample Size** – 80% power to detect 18.5% relative reduction in primary endpoint; 88% participation in QOL questionnaires
 - **sample size decreased and follow-up extended due to slow recruitment
- **Endpoints** – primary outcome: CV mortality, MI, UA, CHF, resuscitated cardiac arrest carefully defined; distribution change in angina determined
 - **endpoints changed from death and MI when event rate low

ISCHEMIA Trial Analysis

- **Conclusions** – Primary endpoint supported by data; QOL customized to angina degree at entry
- **Applicability** – Early invasive strategy not associated with significant reduction in clinical events but more effective in relieving angina; *potential to change clinical practice*

ISCHEMIA Trial Perspectives

- The results of ISCHEMIA provide new data in patients with SIHD and moderate to severe ischemia treated with contemporary GDMT and revascularization techniques.
- Adherence to **GDMT** critically important and challenging to achieve
- Importance and practice of shared decision making is promoted; discuss early and late risks and benefits and what to expect based on degree of angina

Patient Point of View

“Adherence to recommendations can be enhanced by shared decision making between clinicians and patients, with patient engagement in selecting interventions based on individual values, preferences, and associated conditions and comorbidities.”

Shared Decisions



Conservative

- No \uparrow risk of clinical events
- Well controlled angina, delayed Invasive strategy possible; avoid in 2/3 patients
- Late hazard

Invasive

- No \downarrow risk of clinical events
- Less angina; predictable
- Early hazard

ISCHEMIA Trial Perspectives

What More Do We Need to Know?

- **Completeness of revascularization in ischemic territory**
- **Outcomes with achievement of optimal GDMT**
- **Longer term follow-up**
- **Development of tools to help patients predict risks and benefits of each strategy**