Management of Intracranial Atherosclerosis after SAMMPRIS

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Disclosures

• Recipient of Research Funding From the NIH / NINDS for the SAMMPRIS trial (role: Director of Risk Factor Management) and K23 Grant

• SAMMPRIS Industry Support: AstraZeneca supplied Rosuvastatin, Study Devices supplied by Stryker, 3rd party Monitoring of Sites by Stryker
Outline

• Describe the epidemiology of intracranial stenosis

• Describe the SAMMPRIS Trial results and impact on current treatment

• Describe the features of intensive medical management

• Discuss future possible treatments
Importance of Intracranial Atherosclerotic Stenosis

- Based on ethnic and racial make-up of world population, may be most important cause of stroke
- Percent of Strokes Caused by ICAS:
  - Chinese 33–50%, Thailand 47%, Korean 56%, South Asians 54%, Egyptians 27%, USA 8% (Hispanics 11%)
- 90,000 patients with TIA or Stroke / year in USA
- Approximately 50,000 strokes per year at a cost of $750,000,000 in 1 year and $4.5 billion over the lifetime of these patients
- Still Understudied – Only 7 Completed Randomized Trials Dedicated to ICAS
Mechanisms of Stroke

- Plaque rupture with artery-to-artery embolisation
  - Platelet-thrombin emboli

- Plaque overgrowth of perforator artery ostia

- Lacunar stroke

- Hypoperfusion through stenotic artery
  - Watershed or border-zone stroke
Study Design

Angioplasty and Stenting (Self-Expanding Wingspan Stent) + Aggressive Medical Management

VS.

Aggressive Medical Management alone
Main SAMMPRIS Inclusion Criteria

• 70 - 99% stenosis
• Recent (within 30 days) non-disabling stroke or TIA
1. Aspirin 325 mg / Day for Entire Follow-Up
2. Clopidogrel 75mg / Day for 90 Days
3. Aggressive, Protocol Driven Risk Factor Management Primarily Targeting:
   - Systolic Blood Pressure < 140 mm Hg (130 Diabetics) (JNC7)
   - LDL < 70 mg / dl (NCEP ATP III)
4. INTERxVENT – A Lifestyle Modification Program
5. Antihypertensive Agents, Statin, and Antithrombotic Agents Provided to Patients

ALL IMPLEMENTED BY STUDY NEUROLOGISTS AND COORDINATORS

*Turan et al. Circ Cardiovasc Qual Outcomes. 2012;5:e51-e60*
• April 5, 2011: DSMB / NINDS stopped enrollment after 451 patients randomized (target was 764 patients)
Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis

Marc I. Chimowitz, M.B., Ch.B., Michael J. Lynn, M.S., Colin P. Derdeyn, M.D., Tanya N. Turan, M.D., David Fiorella, M.D., Ph.D., Bethany F. Lane, R.N., L. Scott Janis, Ph.D., Helmi L. Lutsep, M.D., Stanley L. Barnwell, M.D., Ph.D., Michael F. Waters, M.D., Ph.D., Brian L. Hoh, M.D., J. Maurice Hourihane, M.D., Elad I. Levy, M.D., Andrei V. Alexandrov, M.D., Mark R. Harrigan, M.D., David Chiu, M.D., Richard P. Klucznik, M.D., Joni M. Clark, M.D., Cameron G. McDougall, M.D., Mark D. Johnson, M.D., G. Lee Pride, Jr., M.D., Michel T. Torbey, M.D., M.P.H., Osama O. Zaidat, M.D., Zoran Rumboldt, M.D., and Harry J. Cloft, M.D., Ph.D., for the SAMMPRIS Trial Investigators*

Data as of April 2011, published September 2011
Primary Endpoint: Any Stroke or Death Within 30 Days of Enrollment or Stroke in Territory Beyond 30 Days

Cumulative Probability of Event

- PTAS - Actual
- Medical - Actual
- Medical - Projected
- PTAS - Projected

$p = 0.009$
Follow up and medical treatment of all enrolled patients was continued for another 2 years – ended April 2013
Primary Endpoint

- Medical group
- PTAS group

Number at risk:

<table>
<thead>
<tr>
<th></th>
<th>Medical group</th>
<th>PTAS group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>227</td>
<td>224</td>
</tr>
<tr>
<td>6 months</td>
<td>199</td>
<td>184</td>
</tr>
<tr>
<td>12 months</td>
<td>185</td>
<td>175</td>
</tr>
<tr>
<td>18 months</td>
<td>180</td>
<td>173</td>
</tr>
<tr>
<td>24 months</td>
<td>172</td>
<td>170</td>
</tr>
<tr>
<td>30 months</td>
<td>132</td>
<td>128</td>
</tr>
<tr>
<td>36 months</td>
<td>92</td>
<td>91</td>
</tr>
<tr>
<td>42 months</td>
<td>47</td>
<td>50</td>
</tr>
<tr>
<td>48 months</td>
<td>12</td>
<td>13</td>
</tr>
</tbody>
</table>

Cumulative probability of the primary endpoint:

- Medical group
- PTAS group

p = 0.0252
Which Components of Medical Rx Resulted in Much Lower Stroke Rate?
Antiplatelet agents
Clopidogrel with Aspirin in Acute Minor Stroke or Transient Ischemic Attack

Yongjun Wang, M.D., Yilong Wang, M.D., Ph.D., Xingquan Zhao, M.D., Ph.D., Liping Liu, M.D., Ph.D., David Wang, D.O., F.A.H.A., F.A.A.N., Chunxue Wang, M.D., Ph.D., Chen Wang, M.D., Hao Li, Ph.D., Xia Meng, M.D., Ph.D., Liying Cui, M.D., Ph.D., Jianping Jia, M.D., Ph.D., Qiang Dong, M.D., Ph.D., Anding Xu, M.D., Ph.D., Jinsheng Zeng, M.D., Ph.D., Yansheng Li, M.D., Ph.D., Zhimin Wang, M.D., Haiqin Xia, M.D., and S. Claiborne Johnston, M.D., Ph.D., for the CHANCE Investigators*
Stroke Recurrence in CHANCE: ICAS vs. Non-ICAS

<table>
<thead>
<tr>
<th>Numbers at risk</th>
<th>ICAS+/A</th>
<th>ICAS+/C+A</th>
<th>ICAS-/C+A</th>
<th>ICAS-/A</th>
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</thead>
<tbody>
<tr>
<td>285</td>
<td>204</td>
<td>219</td>
<td>294</td>
<td></td>
</tr>
<tr>
<td>283</td>
<td>202</td>
<td>216</td>
<td>293</td>
<td></td>
</tr>
<tr>
<td>231</td>
<td>164</td>
<td>179</td>
<td>236</td>
<td></td>
</tr>
<tr>
<td>300</td>
<td>231</td>
<td>250</td>
<td>308</td>
<td></td>
</tr>
</tbody>
</table>

Days from randomization to stroke
CLAIR Study

Lancet Neurol 2010; 9: 489–97

Clopidogrel plus aspirin versus aspirin alone for reducing embolisation in patients with acute symptomatic cerebral or carotid artery stenosis (CLAIR study): a randomised, open-label, blinded-endpoint trial

Ka Sing Lawrence Wong, Christopher Chen, Jianhui Fu, Hui Meng Chang, Nijasri C Suwanwela, Yining N Huang, Zhao Han, Kay Sin Tan, Disya Ratanakorn, Pavithra Chollate, Yudong Zhao, Angeline Koh, Qing Hao, Hugh S Markus, for the CLAIR study investigators*
Clopidogrel Beyond 90 Days: Data From SAMMPRIS Submitted to ISC 2015

<table>
<thead>
<tr>
<th></th>
<th>On Clopidogrel</th>
<th>Off Clopidogrel</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medical Arm</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. Patients</td>
<td>50</td>
<td>158</td>
<td></td>
</tr>
<tr>
<td>Median follow-up (months)</td>
<td>36</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>No. Primary endpoints* (%)</td>
<td>3 (6.0%)</td>
<td>17 (10.8%)</td>
<td>0.31†</td>
</tr>
<tr>
<td>No. Major hemorrhages (%)</td>
<td>2 (4.0%)</td>
<td>4 (2.5%)</td>
<td>0.63‡</td>
</tr>
<tr>
<td><strong>Stenting Arm</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. Patients</td>
<td>46</td>
<td>143</td>
<td></td>
</tr>
<tr>
<td>Median follow-up (months)</td>
<td>34</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>No. Primary endpoints* (%)</td>
<td>4 (8.7%)</td>
<td>14 (9.8%)</td>
<td>0.82†</td>
</tr>
<tr>
<td>No. Major hemorrhages (%)</td>
<td>5 (10.9%)</td>
<td>5 (3.5%)</td>
<td>0.07‡</td>
</tr>
</tbody>
</table>

* ischemic stroke in the territory or any stroke or death within 30 days after revascularization during follow-up
† logrank test
‡ Fisher’s exact test
Management of Risk Factors
Potential Impact of Aggressive Medical Management

<table>
<thead>
<tr>
<th>Clinical Trial</th>
<th>Primary Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any stroke or death within 30 days or stroke in the territory beyond 30 days</td>
</tr>
<tr>
<td><strong>SAMMPRIS</strong></td>
<td>30 days: 5.8%</td>
</tr>
<tr>
<td>• aggressive control</td>
<td>1 year: 12.2%</td>
</tr>
<tr>
<td>of risk factors</td>
<td></td>
</tr>
<tr>
<td>• all received dual</td>
<td></td>
</tr>
<tr>
<td>antiplatelets</td>
<td></td>
</tr>
<tr>
<td>90 days</td>
<td></td>
</tr>
<tr>
<td><strong>WASID</strong></td>
<td>30 days: 10.7%</td>
</tr>
<tr>
<td>• pts meeting SAMMPRIS</td>
<td>1 year: 25%</td>
</tr>
<tr>
<td>• usual control of</td>
<td></td>
</tr>
<tr>
<td>risk factors</td>
<td></td>
</tr>
<tr>
<td>• randomized to warfarin or aspirin</td>
<td></td>
</tr>
</tbody>
</table>

WASID = Warfarin-Aspirin Symptomatic Intracranial Disease Trial
### Percent of Patients Achieving Target Risk Factor Levels in WASID
*(Baseline to Year 2, n=229)*

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Baseline</th>
<th>Year 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP &lt; 140 mm Hg</td>
<td>55%</td>
<td>53%</td>
</tr>
<tr>
<td>LDL &lt; 100 mg/dl</td>
<td>29%</td>
<td>56% ***</td>
</tr>
<tr>
<td>LDL &lt; 70 mg/dl</td>
<td>9%</td>
<td>10%</td>
</tr>
<tr>
<td>Hgb A1C ≤ 7% *****</td>
<td>32%</td>
<td>52% *</td>
</tr>
<tr>
<td>Not Smoking</td>
<td>80%</td>
<td>84% *</td>
</tr>
</tbody>
</table>

*p < 0.05, ** p < 0.01, *** p < 0.001, **** Diabetic patients only*
Risk Factor Control And Major Vascular Events in WASID

Relationship Between Blood Pressure and Stroke Recurrence in Patients With Intracranial Arterial Stenosis
Tanya N. Turan, George Cotsonis, Michael J. Lynn, Seemant Chaturvedi, Marc Chimowitz and for the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) Trial Investigators
_Circulation_ 2007;115;2969-2975; originally published online May 21, 2007;
DOI: 10.1161/CIRCULATIONAHA.106.622464

Risk factor status and vascular events in patients with symptomatic intracranial stenosis
S. Chaturvedi, T. N. Turan, M. J. Lynn, S. E. Kasner, J. Romano, G. Cotsonis, M. Frankel, M. I. Chimowitz and For the WASID Study Group
_Neurology_ 2007;69:2063-2068
DOI: 10.1212/01.wnl.0000279338.18776.26

Figure 1  Risk of stroke, myocardial infarction (MI), or vascular death according to mean systolic blood pressure (SBP)

Figure 2  Risk of stroke, myocardial infarction (MI), or vascular death according to mean cholesterol (CHOL) level
1. Aggressive, Protocol Driven Risk Factor Management Primarily Targeting:
   - Systolic Blood Pressure < 140 mm Hg (130 Diabetics) (JNC7)
   - LDL < 70 mg / dl (NCEP ATP III)

2. Secondary Risk Factor Targets: non-HDL < 100 mg/dl, HgA1c < 7%, BMI < 25 kg/m² (25-27) or 10% weight loss (>27), smoking cessation, exercise (> 30 mins moderate ≥ 3 times per week)

4. INTERxVENT – A Lifestyle Modification Program

5. Antihypertensive Agents, Statin, and Antithrombotic Agents Provided to Patients

Mean LDL and SBP in SAMMPRIS

Achievement of Target Levels

- **LDL (mg/dl)**
- **SBP (mm Hg)**

30 days
Achievement of Target Levels

% of patients meeting risk factor targets in SAMMPRIS

- LDL
- SBP
- smoking
- physical activity
- weight
- HgA1c (diabetics only)

% of patients in target

0 4 8 12 16 20 24 28 32 36

30 days
## Risk Factors Associated with Stroke, MI and Vascular Death in SAMMPRIS

### Medical Group Only

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Event Rate +RF</th>
<th>Event Rate -RF</th>
<th>Hazard Ratio (95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean SBP ≥ 140 mmHg (≥ 130 for diabetics)</td>
<td>29%</td>
<td>17%</td>
<td>1.87 (1.07 - 3.23)</td>
<td>0.0243</td>
</tr>
<tr>
<td>Mean LDL ≥ 70 mg/dL</td>
<td>28%</td>
<td>17%</td>
<td>1.88 (1.06 - 3.34)</td>
<td>0.0285</td>
</tr>
<tr>
<td>Mean HgA1c ≥ 7% (diabetics)</td>
<td>28%</td>
<td>21%</td>
<td>1.39 (0.64 - 3.02)</td>
<td>0.3991</td>
</tr>
<tr>
<td>Mean Non-HDL ≥ 100 mg/dL</td>
<td>28%</td>
<td>19%</td>
<td>1.59 (0.92 - 2.76)</td>
<td>0.0931</td>
</tr>
<tr>
<td>Smoking at any point</td>
<td>20%</td>
<td>24%</td>
<td>0.74 (0.41 - 1.34)</td>
<td>0.3206</td>
</tr>
<tr>
<td>Inadequate exercise (mean PACE score &lt; 4)</td>
<td>33%</td>
<td>10%</td>
<td>4.01 (2.01 - 8.01)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean BMI &gt;25 kg/m² (or mean weight loss &lt;10% if initial BMI &gt;27 kg/m²)</td>
<td>23%</td>
<td>23%</td>
<td>0.97 (0.49 - 1.93)</td>
<td>0.9308</td>
</tr>
</tbody>
</table>
SAMMPRIS

- 70-99% stenosis
- TIA or stroke < 30 days

SBP


WASID

Warfarin vs. Aspirin for Symptomatic Intracranial Disease

- 50-99% stenosis
- TIA or stroke < 90 days

LDL

- 70-99% stenosis
- TIA or stroke < 30 days

TC (total cholesterol)

- 50-99% stenosis
- TIA or stroke < 90 days

Physical Activity

- Physical Activity In Target
- Physical Activity Out of Target

Cumulative Probability of Ischemic Stroke, Myocardial Infarction or Vascular Death

No. at Risk
- In Target: 99, 92, 88, 86, 84, 71, 52, 25, 6
- Out of Target: 128, 101, 87, 82, 76, 50, 30, 15, 2

Months since Randomization
Summary: What We Know And Don’t Know About Risk Factor Management

Know:
• Poor control with usual care
• Good control with aggressive management in a trial
• Achieving BP, LDL, exercise targets >>> Good outcome

Don’t Know:
• ? Real life implementation
Endovascular Therapy
Why Was Stroke Rate So High in Stenting Arm?

Cumulative Probability of Event

Months after Enrollment

PTAS - Actual

PTAS - Projected

SAMMPRIS

Stenting & Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis
Common Peri-Procedural Strokes in SAMMPRIS

Why Hasn’t Stenting Provided Benefit Beyond 30 Days?

Cumulative Probability of a Primary Endpoint

Months after Randomization

# at Risk:

<table>
<thead>
<tr>
<th>Group</th>
<th>Months</th>
<th># at Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Group</td>
<td>0</td>
<td>227</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>196</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>164</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>132</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>115</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>92</td>
</tr>
<tr>
<td>PTAS Group</td>
<td>0</td>
<td>224</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>182</td>
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<td>12</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>83</td>
</tr>
</tbody>
</table>

p = 0.009
<table>
<thead>
<tr>
<th>Period</th>
<th>PTAS</th>
<th>Medical</th>
<th>Absolute RR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Days</td>
<td>14.7%</td>
<td>5.8%</td>
<td>8.9%</td>
<td>0.002</td>
</tr>
<tr>
<td>Year 1</td>
<td>19.7%</td>
<td>12.6%</td>
<td>7.1%</td>
<td>0.04</td>
</tr>
<tr>
<td>Year 2</td>
<td>20.6%</td>
<td>14.1%</td>
<td>6.5%</td>
<td>0.07</td>
</tr>
<tr>
<td>Year 3</td>
<td>23.9%</td>
<td>14.9%</td>
<td>9.0%</td>
<td>0.02</td>
</tr>
</tbody>
</table>
Primary Endpoint

Cumulative probability of the primary endpoint over months since randomisation.

- Medical group
- PTAS group

Number at risk:
- Medical group: 227, 199, 185, 180, 172, 132, 92, 47, 12
- PTAS group: 224, 184, 175, 173, 170, 128, 91, 50, 13

p = 0.0252
VISSIT Trial

- Medical Rx + Stenting with Pharos Stent (balloon expandable stent) vs. Medical Rx
- Similar entrance criteria to SAMMPRIS
- Included European and Asian Sites
VISSIT Trial

• Enrollment stopped early (112 patients)

• 1 yr follow-up data presented at ICAS 2013 / 6th SVIN meeting:
  
  – Rate of primary endpoint (stroke and “hard TIA” in territory) at 1 year significantly higher in stenting group

  – 30-day and 1-year ischemic stroke and ICH rates in stenting arm higher than in SAMMPRIS stenting arm
Why Hasn’t Stenting Provided Benefit Beyond 30 Days?

• Medical Risk Lower Than Expected
  – ? Risk of embolization drops (? Stabilization of plaque with AMM)
  – ? Hypoperfusion is an uncommon mechanism of stroke (perhaps collaterals develop)

• Some Risk in Stented Patients Persists
  – ? Embolization
  – ? Restenosis or late stent thrombosis
Are there subgroups of patients that benefit from Endovascular Therapy?
Qualifying Event on Antithrombotic

Cumulative Probability of a Primary Endpoint

# at Risk:

<table>
<thead>
<tr>
<th></th>
<th>AMM</th>
<th>PTAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>140</td>
<td>144</td>
</tr>
<tr>
<td>3</td>
<td>124</td>
<td>114</td>
</tr>
<tr>
<td>6</td>
<td>105</td>
<td>96</td>
</tr>
<tr>
<td>9</td>
<td>84</td>
<td>78</td>
</tr>
<tr>
<td>12</td>
<td>72</td>
<td>69</td>
</tr>
<tr>
<td>15</td>
<td>55</td>
<td>60</td>
</tr>
</tbody>
</table>

PTAS
Medical

Overall: \( p = 0.028 \)
At 30 Days: \( p = 0.0009 \)
Other subgroups?

- gender,
- age (<60 or ~60 years),
- race (white or black),
- diabetes,
- hypertension,
- lipid disorder,
- smoking status,
- type of qualifying event (QE) (TIA, non-penetrator stroke or penetrator stroke),
- QE hypoperfusion symptoms (related to either change in position, exertion or recent change in antihypertensive),
- use of antithrombotic or proton pump inhibitor at baseline, days to enrollment (S7 or >7),
- old infarcts in the same territory,
- percent stenosis (<80% or ~80%),
- other artery stenosis
- location of the symptomatic artery

In all subgroups, event rates with higher with PTAS than with AAM.
Secondary Prevention For Symptomatic ICAS

Symptomatic Intracranial Atherosclerotic Stenosis

75% of WASID Cohort

< 70% Stenosis Or TIA / Stroke > 30 Days

70-99% Stenosis And TIA / Stroke ≤ 30 Days

Stroke in Territory: 3-9% at 1 Year

- aspirin + intensive risk factor management
- aspirin + clopidogrel + intensive risk factor management
### WASID Stroke in Territory: 70-99% Stenosis and Time from Qualifying Event

<table>
<thead>
<tr>
<th></th>
<th>At 1 Year</th>
<th>At 2 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 30 days</td>
<td>22.9% (95% CI 15.4 – 30.4%)</td>
<td>25% (95% CI 17.2% - 32.9%)</td>
</tr>
<tr>
<td>&gt; 30 days</td>
<td>9% (95% CI 2.1 – 16.0%)</td>
<td>9% (95% CI 2.1 – 16.0%)</td>
</tr>
</tbody>
</table>
Secondary Prevention For Symptomatic ICAS

70-99% Stenosis And TIA / Stroke < 30 Days:
12.2 % at 1 Yr on Med Rx

<12.2% at 1 Yr

>12.2% at 1 Yr
Studies To Identify High-Risk Patients

• Clinical Features
• Biomarkers
• Imaging Predictors
  – Angiographic Collaterals
  – Quantitative MRA
  – Fractional Flow With MRA
  – High Resolution MRI

SAMMPRIS And Other Ongoing Studies Will Provide Important Data in All These Areas
Imaging Predictors of Stroke Risk

Angiographic Collaterals

Quantitative MRA

VFR = 31 mL/min

HR MRI To Identify Intracranial Plaque Features

TOF MRA To Calculate Fractional Flow
Other Therapies?
Will There Be a Role for Endovascular Therapy?

- Hopefully, But The Peri-Procedural Stroke Rate (Perforator Strokes, ICH and SAH) Will Need to Be Lowered
- Unlikely With Stenting Using Current Devices – Enrollment in VISSIT Trial Comparing Pharos Stent With Medical Therapy Also Stopped Early
- ? Angioplasty Alone
Cerebral revascularization with bypass (A) and EDAS (B). In EDAS a network of collaterals forms between the donor artery and the adjacent brain vessels without a surgical anastomosis.
Upper Limb Ischemic Preconditioning For Preventing Stroke in ICAS
Meng et al. Neurology 2012

• Randomized Trial (n=68):
  Brief Repetitive Cycles of Occluding Both Brachial Arteries With a BP Cuff BID x 300 Days vs. Usual Care

• 300 Day Stroke Rate: 7.9% vs. 26.7% (p<0.01)

• Mechanism of Action of Ischemic Preconditioning:
  – ? Improved Cerebral Perfusion and Collaterals
  – ? Platelet Inhibition

• Warrants a Larger Randomized Trial
Summary

• Substantial Progress Has Been Made in Lowering the Risk of Stroke in Patients With ICAS

• Aggressive Medical Management is the Treatment of Choice and is Effective for Most Patients with ICAS

• A Subgroup of Patients With ICAS Fails Aggressive Medical Therapy - This Subgroup Still Accounts For A Large Number of Patients in the USA and Worldwide

• Future Research For ICAS Should Focus On:
  - Identifying Clinical, Biomarker and Imaging Predictors of Increased Stroke Risk
  - Clinical Trials to Test New Therapeutic Strategies For These High Risk Patients
Leadership of SAMMPRIS and WASID

SAMMPRIS Executive

Neurology PI: Marc Chimowtiz MBChB
Neurointerventional PIs:
Colin Derdeyn MD, Dave Fiorella MD PhD
Statistical PI: Mike Lynn MS
Risk Factor Management:
  Tanya Turan MD
Project Manager:
  Bethany Lane BSN, RN,
  Jean Montgomery RN
NIH Project Manager:
  Scott Janis PhD
Administrator:
  Mary Evelyn Armstrong

Steering Committees

SAMMPRIS: Helmi Lutsep, Stan Barnwell, Michael Walters, Brian Hoh, Maurice Hourihane, Elad Levy, Andrei Alexandrov, Mark Harrigan, David Chiu, Richard Klucznik, Joni Clark, Cameron McDougall, Mark Johnson, Lee Pride, Michel Torbey, Osama Zaidat, Harry Cloft

WASID: Barney Stern, Vicki Hertzberg, Harriet Howlett-Smith, Michael Frankel, Steven Levine, Seemant Chaturvedi, Scott Kasner, Curt Benesch, Cathy Sila, Tudor Jovin, Jose Romano
"Take an aspirin every day, but before you swallow it, take it out for a five-mile walk."