PLENARY SESSION
DRUG ELUTING STENT SUMMIT-II

A PACLITAXEL-ELUTING STENT FROM INDIA:
INFINNIUM – SIMPLE 1 TRIAL RESULTS

Prof. D. S. Gambhir  MD, DM
CEO & Director of Cardiology
Kailash Heart Institute,
Noida - INDIA

ANGIOPLASTY SUMMIT 2004, KOREA
April 29, 2004
Balloon Angioplasty

Restenosis

Solutions

Systemic Drug Therapy

Mechanical Devices (Stents)

Brachy - Therapy

Local Delivery of Drugs

Drug-Eluting Stents
Drug-Eluting Stents

- **INFINNIUM (SMT)**
  - Efficacy
  - Limitation

- **CYPHER (J&J)**
  - Established

- **TAXUS (BSC)**
  - High Cost

*Limitation* High Cost
Drug-Eluting Stents

CYPHER

INFINNIUM (SMTPL)

TAXUS

A PACLITAXEL-ELUTING STENT FROM INDIA

Results of SIMPLE-1 Trial in First 282 Patients Treated by Infinnium Paclitaxel-Eluting Stent
**INFINNIUM : PACLITAXEL-ELUTING STENT COMPOSITION**

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent Platform</td>
<td>Millennium stent</td>
</tr>
<tr>
<td></td>
<td>Slotted tube design</td>
</tr>
<tr>
<td>Antiproliferative Drug</td>
<td>Paclitaxel</td>
</tr>
<tr>
<td>Drug Delivery Vehicle</td>
<td>Biodegradable Polymers</td>
</tr>
<tr>
<td>Drug Release</td>
<td>Slow</td>
</tr>
</tbody>
</table>
THE POLYMERS : BIODEGRADABLE

- Four Different Polymers
- Selection Done by Known Medical Application and Favorable Screening *in vitro* and *in vivo*
- Formulated Into Four Layers with Different Composition and Concentration in Each Layer
PERCENTAGE PACLITAXEL IN DIFFERENT COATING LAYERS

- 0% (Protecting Layer)
- 33% (Fast Release)
- 30% (Medium Release)
- 36% (Slow Release)

Stent strut
DRUG LOADING AND RELEASE: 16MM STENT

- Total Drug Content: 180 µgm
- Drug Content in Relation to Stent Surface Area: 3 µgm/mm²

Cumulative Drug Release (3.0 µg/mm²)
CONTROLLED RELEASE PATTERN OF PACLITAXEL FROM POLYMER MATRIX

Drug Released Per Day

Time (Day)
CLINICAL DATA

Safety and Efficacy of InfinniuM

A Paclitaxel-Eluting (SIMPLE 1) Stent

Multicentric Open Label Registry

Results in First 282 Patients
SIMPLE 1 : DEMOGRAPHIC DATA

- No. of Patients : 282
- Period of Implant : Aug.02 – Feb. 03 (7 months)
- Age (Years)
  - Range : 26 – 86
  - Mean : 53.2
- Sex Distribution
  - Males : 234 (83%)
  - Females : 48 (17%)
### SIMPLE 1: RISK FACTOR PROFILE

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>94</td>
<td>33.3%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>83</td>
<td>29.4%</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>70</td>
<td>24.8%</td>
</tr>
<tr>
<td>Smoking</td>
<td>53</td>
<td>18.8%</td>
</tr>
<tr>
<td>Single</td>
<td>105</td>
<td>37.2%</td>
</tr>
<tr>
<td>Multiple</td>
<td>126</td>
<td>44.7%</td>
</tr>
<tr>
<td>None</td>
<td>51</td>
<td>18.1%</td>
</tr>
</tbody>
</table>
SIMPLE 1
CORONARY ARTERY PROFILE

Severity of CAD

- TVD (5%)
- DVD (22.7%)
- SVD (72.3%)
- Others (5.3%)

Target Vessel (N=318)

- RCA (19.2%)
- LCx (13.2%)
- LAD (62.3%)
- Others (5.3%)
SIMPLE 1

INFINNIUM STENTS USED (N = 318)

LENGTH

- Average Stent Length = 18 mm
- Stent Length
  - ≥ 16 mm = 69.8%
  - ≥ 19 mm = 45.6%
Infinnium® Paclitaxel-Eluting Stent

**Follow-up Schedule**

**Patients (N = 282)**

- **Clinical**
  - **Number**
    - **Available**
      - **Timings**
        - One, Three and Six Months FU
  - **100%**

- **Angiographic**
  - **First 100 Patients**
  - Six Months Post-Implant (Av. 6.35 Months)
SIMPLE 1: RESULTS

I. IN-HOSPITAL COMPLICATIONS

- Reocclusion of Target Vs.: 2 (0.7%)
- Myocardial Infarction: 1 (0.35%)
- Death: 2 (0.7%)
- CABG: 0
**II. MACE AT ONE MONTH FU**

<table>
<thead>
<tr>
<th>Event</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subacute Thrombosis</td>
<td>6</td>
<td>2.1%</td>
</tr>
<tr>
<td>Successful Re-PTCA</td>
<td>5</td>
<td>1.8%</td>
</tr>
<tr>
<td>CABG</td>
<td>1</td>
<td>0.35%</td>
</tr>
<tr>
<td>MI</td>
<td>1</td>
<td>0.35%</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td>6</td>
<td><strong>2.1%</strong></td>
</tr>
</tbody>
</table>
### III. MACE BETWEEN ONE AND SIX MONTHS

<table>
<thead>
<tr>
<th>Event</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-Intervention</td>
<td>2</td>
<td>0.71%</td>
</tr>
<tr>
<td>Re-PTCA</td>
<td>2</td>
<td>0.71%</td>
</tr>
<tr>
<td>CABG</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>1</td>
<td>0.35%</td>
</tr>
<tr>
<td>Death</td>
<td>4</td>
<td>1.42%</td>
</tr>
<tr>
<td>Cardiac</td>
<td>2</td>
<td>0.71%</td>
</tr>
<tr>
<td>Non-Cardiac</td>
<td>2</td>
<td>0.71%</td>
</tr>
<tr>
<td>Overall</td>
<td>6</td>
<td>2.12%</td>
</tr>
</tbody>
</table>
SIMPLE 1: RESULTS

IV. OVERALL MACE UPTO SIX MONTHS FOLLOW-UP

- Number of Patients: 282
- MACE: 14 (4.96%)
- Re-PTCA: 7 (2.48%)
- Death: 6 (2.12%)
  - Cardiac: 4 (1.42%)
  - Non-Cardiac: 2 (0.71%)
- MI: 3 (1.06%)
- CABG: 1 (0.35%)

Event-Free Survival: 95%
SIMPLE 1

QUANTITATIVE CORONARY ANGIOGRAPHY

95 patients

94 patients
material received

92 patients
QCA analysis

2 videos not analyzable

2 patients not analyzable

77 Patients
One vessel disease

6 patients
Two vessel disease

2 patients
Three vessel disease
**SIMPLE 1**

**QCA : IN-STENT ANALYSIS**

<table>
<thead>
<tr>
<th></th>
<th>Patients = 85</th>
<th>N = 95 lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion Length (mm)</td>
<td></td>
<td>11.9 ± 4.4</td>
</tr>
<tr>
<td>Reference Diameter (mm)</td>
<td></td>
<td>2.64 ± 0.54</td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>Pre</td>
<td>0.92 ± 0.43</td>
</tr>
<tr>
<td></td>
<td>Post</td>
<td>2.44 ± 0.40</td>
</tr>
<tr>
<td></td>
<td>FU</td>
<td>2.29 ± 0.70</td>
</tr>
<tr>
<td>Late Loss (mm)</td>
<td></td>
<td>0.19 ± 0.68</td>
</tr>
<tr>
<td>Late Loss Index</td>
<td></td>
<td>0.16 ± 0.49</td>
</tr>
<tr>
<td>Diameter Stenosis (%)</td>
<td>FU</td>
<td>18.8 ± 18.7</td>
</tr>
<tr>
<td>Restenosis Rate (%)</td>
<td></td>
<td>6.3</td>
</tr>
</tbody>
</table>

N = 95 lesions

Patients = 85
**QCA: PERISTENT ANALYSIS**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Post</th>
<th>FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLD (mm)</td>
<td>2.07 ± 0.41</td>
<td>1.99 ± 0.63</td>
</tr>
<tr>
<td>Late Loss (mm)</td>
<td>0.12 ± 0.59</td>
<td></td>
</tr>
<tr>
<td>Late Loss Index</td>
<td>0.11 ± 0.60</td>
<td></td>
</tr>
<tr>
<td>Diameter Stenosis (%)</td>
<td>28.7 ± 17.5</td>
<td></td>
</tr>
<tr>
<td>Restenosis Rate (%)</td>
<td>9.5</td>
<td></td>
</tr>
</tbody>
</table>

Patients = 85

N = 95 lesions
<table>
<thead>
<tr>
<th></th>
<th>Proximal</th>
<th>In-Stent</th>
<th>Distal</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLD (Post)</td>
<td>2.55±0.54</td>
<td>2.44±0.40</td>
<td>2.17±0.49</td>
</tr>
<tr>
<td>MLD (Fup)</td>
<td>2.49±0.70</td>
<td>2.29±0.70</td>
<td>2.16±0.68</td>
</tr>
<tr>
<td>Late Loss</td>
<td>0.08±0.64</td>
<td>0.19±0.68</td>
<td>0.04±0.55</td>
</tr>
<tr>
<td>DS% (Post)</td>
<td>13.9±10.0</td>
<td>12.0±9.16</td>
<td>19.1±11.4</td>
</tr>
<tr>
<td>DS% (FUP)</td>
<td>16.7±18.2</td>
<td>18.8±18.7</td>
<td>20.1±17.2</td>
</tr>
<tr>
<td>Restenosis (%)</td>
<td>2.1</td>
<td>6.3</td>
<td>1.1</td>
</tr>
</tbody>
</table>
IN-STENT ANALYSIS: CUMULATIVE FREQUENCY CURVE
DIAMETER STENOSIS: PRE-, POST PROCEDURE AND FUP

Pre: mean = 64.8%
Post: mean = 12.0%
Fup: mean = 18.8%
**SIMPLE 1**

**IN-STENT ANALYSIS:** CUMULATIVE FREQUENCY CURVE

**MINIMAL LUMEN DIAM.:** PRE-, POST PROCEDURE AND FUP

- **Pre:** mean = 0.92 mm
- **Post:** mean = 2.44 mm
- **Fup:** mean = 2.29 mm
SIMPLE 1

PERI-STENT ANALYSIS: CUMULATIVE FREQUENCY CURVE
DIAMETER STENOSIS: PRE-, POST PROCEDURE AND FUP

- **Pre**: mean = 64.8%
- **Post**: mean = 23.2%
- **Fup**: mean = 28.7%
SIMPLE 1

PERI-STENT ANALYSIS: CUMULATIVE FREQUENCY CURVE
MINIMAL LUMEN DIAM.: PRE-, POST PROCEDURE AND FUP

Pre: mean = 0.92 mm
Post: mean = 2.07 mm
Fup: mean = 1.99 mm
LAD OSTIAL STENOSIS TREATMENT BY INFINNIUM STENT
PROXIMAL LAD STENOSIS TREATMENT BY INFINNIUM STENT
INSTENT RESTENOSIS IN LAD
TREATMENT BY INFINNIUM STENT
TREATMENT OF CTO IN LAD BY OVERLAPPING INFINTIUM STENTS
TANDEM LESIONS IN MID AND DISTAL RCA
TREATMENT BY TWO INFINNIUM STENTS
STENTING OF LONG LESION IN LAD AND BIFURCATION STENOSIS IN RAMUS

- **LAD Long Stenosis**: 70-80%
- **RAMUS (Bifurcation)**: 70-80%
- **Infinnium Stent**
  - LAD (Px / Mid): 3 x 29 mm
  - LAD (Distal): 2.5 x 29 mm
  - RAMUS (Sup. Br.): 2.75 x 19 mm
  - (Inf. Br.): 3 x 23 mm
- **Follow-up Angio**: No Restenosis in After Six Months
  - LAD and RAMUS
## COMPARISON WITH OTHER TRIALS ON DES

### BASELINE CHARACTERISTICS

<table>
<thead>
<tr>
<th>Feature</th>
<th>RAVEL</th>
<th>SIRIUS</th>
<th>TAXUS-II SR / MR</th>
<th>SIMPLE 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Pts.</td>
<td>120</td>
<td>533</td>
<td>131 / 135</td>
<td>282</td>
</tr>
<tr>
<td>Diabetics (%)</td>
<td>15.8</td>
<td>24.6</td>
<td>11 / 17</td>
<td>33.3%</td>
</tr>
<tr>
<td>Lesion Length (mm)</td>
<td>9.6</td>
<td>14.4</td>
<td>10.5 / 10.7</td>
<td>11.9 ± 4.4</td>
</tr>
<tr>
<td>RVD (mm)</td>
<td>2.60</td>
<td>2.78</td>
<td>2.78 / 2.73</td>
<td>2.64 ± 0.54</td>
</tr>
</tbody>
</table>
# COMPARISON WITH OTHER TRIALS ON DES

## CLINICAL AND QCA RESULTS

<table>
<thead>
<tr>
<th>Feature</th>
<th>RAVEL</th>
<th>SIRIUS</th>
<th>TAXUS-II SR / MR</th>
<th>SIMPLE 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Late Loss (mm)</strong></td>
<td>-0.01</td>
<td>0.17</td>
<td>0.31 / 0.30</td>
<td>0.19</td>
</tr>
<tr>
<td><strong>Binary RS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>➡ Instent</td>
<td>0</td>
<td>3.2</td>
<td>2.3 / 4.7</td>
<td>6.3</td>
</tr>
<tr>
<td>➡ Persistent</td>
<td>0</td>
<td>8.9</td>
<td>5.5 / 8.6</td>
<td>9.5</td>
</tr>
<tr>
<td><strong>MACE upto 6 to 9 Months (%)</strong></td>
<td>3.3</td>
<td>4.9</td>
<td>8.5 / 7.8</td>
<td>5%</td>
</tr>
<tr>
<td><strong>TLR / TVR</strong></td>
<td>0.8</td>
<td>3.9</td>
<td>7.7 / 6.2</td>
<td></td>
</tr>
</tbody>
</table>

**COMPARISON WITH OTHER TRIALS ON DES**

**CLINICAL AND QCA RESULTS**

- **Late Loss (mm)**
  - RAVEL: -0.01
  - SIRIUS: 0.17
  - TAXUS-II SR / MR: 0.31 / 0.30
  - SIMPLE 1: 0.19

- **Binary RS**
  - Instent: 0
  - Persistent: 0

- **MACE upto 6 to 9 Months (%)**
  - RAVEL: 3.3
  - SIRIUS: 4.9
  - TAXUS-II SR / MR: 8.5 / 7.8
  - SIMPLE 1: 5%

- **TLR / TVR**
  - RAVEL: 0.8
  - SIRIUS: 3.9
  - TAXUS-II SR / MR: 7.7 / 6.2
  - SIMPLE 1: 0.19
SIMPLE 1

LATE LOSS IN DRUG-ELUTING STENT TRIALS

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>Rapamycin</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAVEL</td>
<td>n=120</td>
<td>n=118</td>
</tr>
<tr>
<td>SIRIUS</td>
<td>n=533</td>
<td>n=525</td>
</tr>
<tr>
<td>ELUTES (Hi)</td>
<td>n=32</td>
<td>n=34</td>
</tr>
<tr>
<td>ASPECT (Hi)</td>
<td>n=60</td>
<td>n=59</td>
</tr>
<tr>
<td>TAXUS-II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SR n=131</td>
<td>0.31</td>
<td>1.04</td>
</tr>
<tr>
<td>MR n=135</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>SIMPLE 1</td>
<td>n=95</td>
<td></td>
</tr>
</tbody>
</table>

Late Loss

-2 -1.5 -1 -0.5 0 0.5 1 1.5 2 mm

ASPECT (Hi) ELUTES (Hi)
QCA: LATE LOSS IN COMPARISON WITH TAXUS II
STENTED AREA AND EDGES

**SIMPLE 1**

Late Loss (mm)

<table>
<thead>
<tr>
<th>Location</th>
<th>Infinnium</th>
<th>Taxus – SR</th>
<th>Taxus – MR</th>
<th>Taxus – Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prox Edge</td>
<td>0.08</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-Stent</td>
<td>0.19</td>
<td>0.31</td>
<td>0.78</td>
<td></td>
</tr>
<tr>
<td>Distal Edge</td>
<td>0.04</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
SUMMARY AND CONCLUSIONS

- First Indigenously Designed and Evaluated DES from Asia
- Safety and Efficacy Comparable to Other DES
  - Cypher and Taxus Marketed in World
- SIMPLE 1 Registry: Data Collected from Non-Selective
  Implantation in Real World Lesions
  - Smaller Vessels / Longer Lesions / Diabetics
- Less Costly Compared to Cypher and Taxus
- Prospective, Multicentric Trial Planned to Start in May 2004
ACKNOWLEDGEMENTS

Sincere Thanks

- Sahajanand Medical Technologies
  - Dhiraj Lal, Chairman
  - Rajesh Vaishnav, Director
  - Manish Doshi, Director
  - Ms Varsha, Co-ordinator
  - Ms Richa, Co-ordinator

- Cardialysis
  - Prof. Patrick Serruys
  - Ms. Marie – angele Morel
  - Ms Patricia C. Otto-Terlouw

- Others
  - Implanting Physicians
  - Patients for their Participation