Clinical Program Summary of Conor Technology

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Columbia University Medical Center
Director, Data Coordinating and Analysis Center
Cardiovascular Research Foundation
New York, NY
## CoStar Clinical Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PISCES</td>
<td>FIM Study, 6-arm dose ranging, clinical endpoint</td>
</tr>
<tr>
<td>CoStar I</td>
<td>Dose Optimization Study, 3-arm optimization, angiographic endpoint</td>
</tr>
<tr>
<td>EuroSTAR</td>
<td>International Pivotal Study, non-randomized, 2-arm, angiographic endpoint</td>
</tr>
<tr>
<td>CoStar II</td>
<td>US Pivotal Study, RCT, 2-arm, clinical and angiographic endpoints</td>
</tr>
</tbody>
</table>
PISCES
Paclitaxel In-Stent Controlled Elution Study

Patrick W. Serruys, MD, PhD, FACC
Principal Investigator
Thoraxcentre - Erasmus University
Rotterdam, The Netherlands

4 and 12-Month Results
PISCES Trial
Study Design & Patient Follow-Up

Prospective non-randomized, dose finding study
Ten participating centers (n=191)

Treatment Arms

U.S. Pivotal and O.U.S. Commercial Dose

D 1
10 µg / 5 days
Bi-Directional
N = 30 patients

D 2
10 µg / 10 days
Bi-Directional
N = 31 patients

D 3
10 µg / 10 days
Mural
N = 30 patients

D 4
30 µg / 10 days
Bi-Directional
N = 31 patients

D 5
10 µg / 30 days
Mural
N = 39 patients

D 6
30 µg / 30 days
Mural
N = 30 patients

Baseline Angiography

1 Month Clinical

4 Month Clinical

4 Month Angiographic with QCA & IVUS

1 Year Clinical

12 Month Angiographic with QCA & IVUS

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A Bi-Directional = direction of paclitaxel elution is both mural and luminal

B 12 Month Angiography w/ QCA and IVUS was optional
# PISCES Trial

## Procedural Outcomes by Dose Group

<table>
<thead>
<tr>
<th>Treatment Arms Formulations</th>
<th>Dose 1 10µg/5d/B</th>
<th>Dose 1 10µg/10d/B</th>
<th>Dose 3 10µg/10d/M</th>
<th>Dose 4 30µg/10d/B</th>
<th>Dose 5 10µg/30d/M</th>
<th>Dose 6 30µg/30d/M</th>
</tr>
</thead>
<tbody>
<tr>
<td># of Patients</td>
<td>N=30</td>
<td>N=31</td>
<td>N=30</td>
<td>N=31</td>
<td>N=39</td>
<td>N=30</td>
</tr>
<tr>
<td># Stents Implanted</td>
<td>N=35</td>
<td>N=33</td>
<td>N=34</td>
<td>N=32</td>
<td>N=45</td>
<td>N=29</td>
</tr>
<tr>
<td>Technical Success</td>
<td>100.0%</td>
<td>90.3%</td>
<td>93.3%</td>
<td>96.8%</td>
<td>97.4%</td>
<td>93.3%</td>
</tr>
<tr>
<td>Procedural Success</td>
<td>93.3%</td>
<td>87.1%</td>
<td>93.3%</td>
<td>96.8%</td>
<td>94.9%</td>
<td>93.3%</td>
</tr>
<tr>
<td>Direct Stenting</td>
<td>50.0%</td>
<td>51.7%</td>
<td>30.0%</td>
<td>70.0%</td>
<td>41.0%</td>
<td>62.1%</td>
</tr>
<tr>
<td>Final Diameter Stenosis</td>
<td>7.5%</td>
<td>5.4%</td>
<td>5.9%</td>
<td>2.1%</td>
<td>2.2%</td>
<td>3.0%</td>
</tr>
</tbody>
</table>

[a] Fisher’s Exact Test used  
[b] Likelihood ratio chi-square test  
[d] F-Test from General Linear Model (GLM)
# PISCES Trial
## 12 Month Outcomes

<table>
<thead>
<tr>
<th>Treatment Arms Formulations</th>
<th>Dose 1 10µg/5d/B</th>
<th>Dose 1 10µg/10d/B</th>
<th>Dose 3 10µg/10d/M</th>
<th>Dose 4 30µg/10d/B</th>
<th>Dose 5 10µg/30d/M</th>
<th>Dose 6 30µg/30d/M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative MACE (Implant to 12 Months)</td>
<td>16.7%</td>
<td>10.3%</td>
<td>10.0%</td>
<td>9.7%</td>
<td>5.1%</td>
<td>6.9%</td>
</tr>
<tr>
<td>In-Segment Late Loss (mm) (12 Months)</td>
<td>0.48</td>
<td>0.51</td>
<td>0.56</td>
<td>0.35</td>
<td>0.30</td>
<td>0.24</td>
</tr>
<tr>
<td>Stent Thrombosis (0 - &lt;6 Months)</td>
<td>0.0% (0/30)</td>
<td>0.0% (0/29)</td>
<td>0.0% (0/30)</td>
<td>0.0% (0/31)</td>
<td>0.0% (0/39)</td>
<td>3.4% (1/29)</td>
</tr>
<tr>
<td>Stent Thrombosis (6 -12 Months)</td>
<td>0.0% (0/30)</td>
<td>0.0% (0/29)</td>
<td>0.0% (0/30)</td>
<td>0.0% (0/31)</td>
<td>0.0% (0/39)</td>
<td>0.0% (0/29)</td>
</tr>
</tbody>
</table>
COSTAR I Trial
COBalt Chromium STent with Anti-Proliferative for Restenosis in India

Dr. Upendra Kaul
Principal Investigator
Batra Hospital & Medical Research Center
New Delhi, India

4 Month & 12 Month Results
COSTAR I Trial
Study Design & Patient Follow-Up

Prospective non-randomized, sequential enrollment.
Extended indication study. Vessel caliber <2.5mm (n=87)

Group 1
30 µg PTX / 10 days*
Bi-Directional Release
N = 10 patients

Group 2
10 µg PTX / 30 days*
Mural Release
N = 40 patients

Group 3
3 µg PTX / 30 days*
Mural Release
N = 37 patients

Baseline Angiography
4 Month Clinical
4 Month Angiography with QCA & IVUS
12 Month Angiography with QCA & IVUS
12 Month Clinical

* in vitro
### COSTAR I Trial
#### 12 Month Outcomes

<table>
<thead>
<tr>
<th>Treatment Arms Formulations</th>
<th>Group 1 30µg/10d/B</th>
<th>Group 2 10µg/30d/M</th>
<th>Group 3 3µg/30d/M</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cumulative MACE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Implant to 12 Months)</td>
<td>20.0%</td>
<td>7.5%</td>
<td>21.6%</td>
</tr>
<tr>
<td><strong>In-Segment Late Loss (mm)</strong></td>
<td>0.76</td>
<td>0.25</td>
<td>0.46</td>
</tr>
<tr>
<td>(12 Months)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Stent Thrombosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0 - &lt;6 Months)</td>
<td>10.0% (1/10)</td>
<td>0.0% (0/40)</td>
<td>5.4% (2/37)</td>
</tr>
<tr>
<td><strong>Stent Thrombosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(6 - 12 Months)</td>
<td>0.0% (0/10)</td>
<td>0.0% (0/40)</td>
<td>0.0% (0/37)</td>
</tr>
</tbody>
</table>

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A Q-Wave MI at day 7 adjudicated as evidence of stent thrombosis (angiographic evidence of total occlusion at 4 month follow-up).

B Two events were adjudicated as evidence of stent thrombosis; one subject who presented with Q-Wave MI at day 5 and one subject who presented with Q-Wave MI at day 11 and cardiac death at day 25 (angiographic follow-up not completed).
EuroSTAR
The European Cobalt Stent with Antiproliferative for Restenosis Trial

Results for Arm 1 (24 Month)
Results for Arm 2 (12 Month)

Principal Investigators:

Keith D. Dawkins M.D. – Southampton University Hospital
Antonio Colombo M.D. – HSR San Raffaele Hospital
EuroSTAR Trial
Study Design & Patient Follow-Up

Prospective, multi-center study, enrolled patients from 18 centers in 6 countries into one of two registry arms. Two different dose formulations of paclitaxel (n=282)

Arm 1
10 µg / 30 days / Mural
N = 145 patients

Baseline Angiography
1 Month Clinical
6 Month Clinical
6 Month Angiography with QCA
1 Year Clinical
Yearly Clinical to 5 Yrs (Arm 1 only)

Arm 2
30 µg / 30 days / Mural
N = 137 patients

Baseline Angiography
1 Month Clinical
6 Month Clinical
6 Month Angiography with QCA
1 Year Clinical
Yearly Clinical to 5 Yrs (Arm 1 only)

U.S. Pivotal and O.U.S. Commercial Dose
# EuroSTAR Trial
## 24 Month Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Arm 1 10µg/30d/M</th>
<th>Arm 2 30 µg/30d/M</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cumulative MACE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Implant to 12 Months)</td>
<td>8.3%</td>
<td>10.2%</td>
</tr>
<tr>
<td><strong>In-Segment Late Loss (mm)</strong>&lt;sup&gt;A&lt;/sup&gt; (6 Months)</td>
<td>0.06</td>
<td>0.19</td>
</tr>
<tr>
<td><strong>Stent Thrombosis</strong> (0 - &lt;6 Months)</td>
<td>1.4%</td>
<td>0.7%</td>
</tr>
<tr>
<td><strong>Stent Thrombosis</strong> (6 -12 Months)</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td><strong>Cumulative MACE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Implant to 24 Months)</td>
<td>10.4%</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Stent Thrombosis</strong> (12 –24 Months)</td>
<td>0.0%</td>
<td>n/a</td>
</tr>
</tbody>
</table>

<sup>A</sup> Per-protocol matched 6 month analysis
COSTAR II Trial
CObalt Chromium STent with Anti-Proliferative for Restenosis II Trial

Principal Investigators
Dean Kereiakes, MD, FACC
Ohio Heart Health Center
Cincinnati, Ohio
Mitchell Krucoff, MD, FACC
Duke University Medical Center
Durham, North Carolina
William Wijns, MD, PhD
OLV Hospital
Aalst, Belgium
Not Just Another DES Study

- First “Real World” clinical trial
- First randomized MV DES study
- Evaluation of HgA1c as a predictor of outcomes
**COSTAR II Trial**

Prospective, Randomized, Single-Blind, Non-Inferiority

- **CoStar Arm**
  - n=989 patients
  - Single De Novo Native Coronary Artery Lesions
  - Reference Vessel Diameter: 2.5 - 3.5 mm
  - Lesion Length: ≤30 mm
  - Pre-dilatation Required

- **TAXUS Arm**
  - n=686 patients
  - 1,675 Total Patients Randomized 3:2
  - 79% (1,330) Single Vessel – 21% (345) Multi-Vessel
  - 30 Day Clinical Follow-up 99.9%
  - 71 Sites in USA, Europe, and New Zealand

**Primary Endpoint: 8-Month MACE**
- Sub-Studies: QCA, IVUS and pK
- Dual antiplatelet therapy for 6 mo.

**322 Day Enrollment**
- 30 Day
- 8 Mo.
- 9 Mo.
- 1 Yr.
- 2 Yr.
- 3 Yr.
- 4 Yr.
- 5 Yr.

Angio (n=350), IVUS (n=70), pK (n=45)
Angio/IVUS for overlapping stents
COSTAR II Trial
Study Flow

Patients Randomized Prior to Predilation
N=1,700

COSTAR n=989
Baseline n=1,675
TAXUS n=686

De-registered n=25

pK n=45
Multi-Vessel Angio n=200
Single Vessel n=150

Single Vessel n=29
Multi-Vessel n=16
IVUS n=70

Single Vessel n=29
Multi-Vessel n=16
IVUS n=70
Study Objective
- Evaluate the safety and efficacy of the CoStar Paclitaxel-Eluting Coronary Stent System in de novo lesions of native coronary arteries

Primary Clinical Endpoint
- Major Adverse Cardiac Events (MACE) at 8 months

Consistency Angiographic Endpoint
- In-segment late lumen loss at 9 months

Blinded Aggregate Subset Analysis
- Outcomes by diabetes mellitus (DM) stratum; all DM, Non-DM, Non-diagnosed DM with elevated Hb A1c >6.5%, IDDM, and NIDDM
- Outcomes by vessel stratum
- Outcomes by overlap and non-overlap stratum
COSTAR II Trial
Key Inclusion/Exclusion Criteria

Inclusion
- Planned single de novo target lesion intervention
- 1, 2, or 3 native coronary vessel(s)
- Target lesion covered by one study stent
- Target lesion ≥2.5 to ≤3.5 mm diameter, length ≤30 mm, with ≥50 and <100% stenosis
- Target vessel has not undergone prior revascularization ≤6 months or has had a DES placed in coronary vessel proximal to target lesion

Exclusion
- MI within 72 hours prior to the index procedure and/or CK >2 times upper limits of normal and elevated MB
- Significant stenosis >50% - protected or not
- Target lesion is ostial in location (≤3.0 mm of vessel origin)
- Target lesion is totally occluded (TIMI flow ≤1)
COSTAR II Trial

30-Day Blinded Aggregate Results
COSTAR II Trial
Baseline Patient Characteristics

Number of Lesions Treated
- One: 80.6%
- Two: 17.3%
- Three or More: 2.2%

ACC/AHA Lesion Classification
- A: 19.9%
- B1: 4.3%
- B2: 56.4%
- C: 19.4%
COSTAR II Trial
Baseline Lesion Location

COSTAR II Overall

Single Vessel Patients = 79%
Multi-Vessel Patients = 21%

LAD 40.4%
LCX 31.1%
RCA 28.3%

LAD 42.1%
LCX 31.3%
RCA 26.3%

LAD 37.0%
LCX 30.7%
RCA 32.3%
## COSTAR II Trial

### Aggregate Index QCA Analysis

<table>
<thead>
<tr>
<th></th>
<th>Blinded Aggregate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-Procedure Quantitative Angiographic Measurements</strong></td>
<td></td>
</tr>
<tr>
<td>Lesion Length (mm)</td>
<td>15.23 ± 6.39</td>
</tr>
<tr>
<td>Reference Vessel Diameter (RVD, in mm)</td>
<td>2.76 ± 0.48</td>
</tr>
<tr>
<td>Minimum Lumen Diameter (MLD, in mm)</td>
<td>0.87 ± 0.41</td>
</tr>
<tr>
<td>Percent Diameter Stenosis (% DS)</td>
<td>68.48 ± 13.46</td>
</tr>
<tr>
<td><strong>Final Quantitative Angiographic Measurements</strong></td>
<td></td>
</tr>
<tr>
<td>Reference Vessel Diameter (RVD, in mm)</td>
<td>2.83 ± 0.48</td>
</tr>
<tr>
<td>In-Segment Minimum Lumen Diameter (MLD, in mm)</td>
<td>2.37 ± 0.48</td>
</tr>
<tr>
<td>In-Segment Percent Diameter Stenosis (% DS)</td>
<td>16.32 ± 8.67</td>
</tr>
<tr>
<td>In-Stent Minimum Lumen Diameter (MLD, in mm)</td>
<td>2.70 ± 0.43</td>
</tr>
<tr>
<td>In-Stent Percent Diameter Stenosis (% DS)</td>
<td>5.93 ± 5.61</td>
</tr>
<tr>
<td>In-Segment Acute Gain (mm)</td>
<td>1.50 ± 0.54</td>
</tr>
<tr>
<td>In-Stent Acute Gain (mm)</td>
<td>1.83 ± 0.49</td>
</tr>
</tbody>
</table>
COSTAR II Trial
Aggregate Blinded COSTAR II 30 Day MACE

- MACE
- Cardiac Death
- QMI
- NQMI
- Clinically Driven TVR
- Clinically Driven TLR
- Stent Thrombosis

Percent (%):
- MACE: 2.2%
- Cardiac Death: 0.6%
- QMI: 2.8%
- NQMI: 0.0%
- Clinically Driven TVR: 0.1%
- Clinically Driven TLR: 0.1%
- Stent Thrombosis: 0.2%

In-Hospital 30 Days Total MACE
COSTAR II Trial
Preliminary Aggregate 30-day Conclusions

- Unique study design for pivotal DES appears to have captured a cohort representative of wider “real world” DES experience
- Blinded baseline demographics are similar between groups
- Baseline RVD by QCA is 2.76mm and lesion length is 15.23mm
- Aggregate blinded 30 Day MACE rate is 2.8%
  - Mostly driven by non-Q MI
  - increased in IDDM, multi-vessel and overlapping stent populations
- 30 Day stent thrombosis is 0.2%

Presented by Dr. Mitchell W. Krucoff, MD, FACC
TCT October, 2006
CoStar II Data Presentation

PCR 2007 in Barcelona
The GENESIS Trial

A Randomized, Multi-center study of the Pimecrolimus-Eluting and Paclitaxel-ElutinG Coronary Stent System in PatiENts with De Novo LEsionS of the Native Coronary ArterIeS

Principal Investigators

Dr. Keith Dawkins
Southampton, United Kingdom

Dr. Stefan Verheye
Antwerp, Belgium
Trial Objective

Primary analysis includes two independent analyses:

two treatment arms compared to a single concurrent control arm

- Demonstrate non-inferiority in 6-month late loss of the Corio™ Pimecrolimus-Eluting Stent compared to the active control arm (CoStar® Paclitaxel-Eluting Coronary Stent)

- Demonstrate non-inferiority in 6-month late loss of the SymBio™ Pimecrolimus/Paclitaxel-Eluting Coronary Stent to the active control arm (CoStar Paclitaxel-Eluting Coronary Stent)
**GENESIS Trial**

Prospective, Three-arm, Asymmetric Randomization (2:2:1)

- Single *De Novo* Native Coronary Artery Lesions
  - Reference Vessel Diameters: 2.5 - 3.5 mm
  - Lesion Length: <25 mm
  - Sites in UK, Belgium, France, Germany and Israel

**Corio™**

Pimecrolimus-Eluting Stent

N = 150 patients

**CoStar®**

Paclitaxel-Eluting Stent

(CE Marked)

N = 75 patients

**SymBio™**

Pimecrolimus/Paclitaxel-Eluting Stent

N = 150 patients

Primary Endpoint: 6-Month In-Stent Late Loss

Sub-Studies:
- 6-Month IVUS (first 30 pts. for each arm)
- Dual antiplatelet therapy for 6 mo.

- Clinical/MACE
  - 30 Day
  - 6 Mo.
  - 1 Yr.
  - 2 Yr.
  - 3 Yr.
  - 4 Yr.
  - 5 Yr.

- Angiographic/IVUS
Safety and Efficacy Endpoints

Primary Endpoint
- Non-inferiority of in-stent late loss at six months
  - Pimecrolimus compared to CoStar
  - Dual pimecrolimus/paclitaxel compared to CoStar

Secondary Endpoints
- Major Adverse Cardiac Event (MACE)
  - 30 d, 6 mo, 1 through 5 year follow-up
- Device, Lesion and Procedure Success
- In-segment late loss
- In-stent and in-segment MLD and binary restenosis
- % Volume Obstruction
- Late acquired stent malapposition
## GENESIS Trial Population

### Major Inclusion Criteria
- Treatment of a single de novo lesion
  - Lesion length < 25 mm
  - RVD between 2.5 mm – 3.5 mm
- Lesion coverable with a single study stent (bailout stenting permitted)

### Major Exclusion Criteria
- Acute MI ≤ 72 hours
- LVEF < 25%
- Left main disease
- Prior revascularization of Target Vessel within preceding 6 months
- Target lesion involves bifurcation requiring treatment
- Angiographic evidence of thrombus
Conor Program has evolved from early dose finding studies to US pivotal trial with the largest and most broad inclusion of patients with CAD undergoing DES

The platform allows for combination therapies and innovative approaches for special patient population

The future is bright for this technology as this technology is truly NEXT Generation!