Coronary Stent Innovation: EPC Capture

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Disclosure Statement of Financial Interest

I, Stephen Rowland, am an employee of OrbusNeich Medical, Inc.
The COMBO Plus Dual Therapy Stent: Abluminal Bioresorbable Drug Delivery with Luminal EPC Capture

Stent & Delivery System
Highly conformable stent with excellent radial strength

Sirolimus & Polymer Matrix
Abluminal drug and bioabsorbable polymer matrix for control proliferation

CD34 Antibodies
Enable active capture of EPC for fast endothelial coverage
CD34 antibodies capture circulating EPCs which mature into functional endothelium.

Following implantation, the immobilized CD34 antibodies are exposed to the circulating blood.

Circulating endothelial progenitor cells (EPC) are captured by antibody.

EPCs attach and differentiate into mature endothelial cells; an important step in re-establishing healthy neointima.
HARMONEE

- HBD WG1 Global Clinical Trial
  - Adopted as Proof-of-Concept Project
- Single Protocol and Data Management
- Parallel trial approval process by PMDA & FDA
- Regulatory Objectives
  - Japan Shonin (market approval)
  - Satisfy US feasibility & invasive follow up requirements
Simultaneous Japan and US trial approval

- Parallel consultation pathways
- Differing consultation processes
  - PMDA – formal presentation, informal consultations on areas of concern, formal submission
  - FDA – informal consultation, formal submission, formal consultations
- Global harmonization initiative – IMDRF
  - HBD experience invaluable preparation
Challenges in Trial Design

• Device Effectiveness
  – Clinical
  – Angiographic
  – Mechanistic

• Device Safety
  – Clinical
  – HAMA

• Differences in clinical practice
HARMONEE Study

Enrollment Cohort Flow Diagram

Inclusion/Exclusion Criteria and Consent
N=572*
Randomized 1:1 Combo vs. EES

1 Year Study Endpoints

Cohort A (N=30)
- Serial 6 & 12 mos OCT,
- 12M QCA, FFR
  Combo N=15 & EES N=15

Cohort B (N=110)
- 12M QCA, OCT, and FFR
- HAMA Baseline, 30 dy, 12M
  Combo N=55 & EES N=55

Cohort C (N=432)
- 12M Angio/FFR only
  Combo N=216 & EES N=216

Primary Endpoint
Ischemia & FFR driven TVF
N=572*

Early & Late OCT Observational
N=30

Intimal Tissue Coverage
Superiority
N=140

HAMA Observational
N=110

*Includes an assumed 5% 1 yr lost to F/U

AHJ 187 112-121 2017; Kong et al.
HARMONEE Status

• Protocol CTN approval by PMDA
• IDE approval by FDA
• 33 Japan sites and 17 US sites
• Enrollment completed June 2016
  • Japan enrollment – 439 subjects
  • US enrollment – 133 subjects
• 12-month follow-up period
  – Completed July 2017
• Primary study results presented as a First Report in the Main Arena at TCT 2017
Harmonized Assessment by Randomized Multicenter Study of OrbusNEich’s COMBO StEnt

The *HARMONEE* Primary Study Report

*Mitchell W. Krucoff MD, FACC, FAHA, FSCAI*

Professor of Medicine / Cardiology
Duke University Medical Center
Director, Cardiovascular Devices Unit
Duke Clinical Research Institute

*on behalf of the Japan-USA HARMONEE investigators*
Enrollment & Follow-Up: ITT population

- 33 sites, 439 pts (77%)
- 572 patients randomized
- 17 sites, 133 pts (23%)

287 COMBO
- 3 (1.0%) non-protocol stent
- 2 (0.7%) withdrew or lost to FU
- 285 (99.3%) 1 year clinical FU
- 271 (95.1%) 1 year angio FU
- 261 (91.6%) 1 year FFR
- Cohort A&B 1 year OCT FU (n=70)
  - 65 (92.9%)

285 EES
- 2 (0.7%) non-protocol stent
- 6 (2.1%) withdrew or lost to FU
- 279 (97.9%) 1 year clinical FU
- 262 (93.9%) 1 year angio FU
- 256 (91.8%) 1 year FFR
- Cohort A&B 1 year OCT FU (n=70)
  - 63 (90.0%)
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Cohort A&B 1 year OCT FU (n=70)

63 (90.0%)

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1 yr Clinical FU 98.6%

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Protocol Imaging
- Angio FU 94.5%
- FFR FU 91.7%
- OCT FU 91.4%

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Duke Clinical Research Institute
From Thought Leadership to Clinical Practice

HARMONEE
HARMONEE 12-mo Trial Results

• Efficacy
  • Met non-inferiority in 12-month Target Vessel Failure [TVF] with 7.0% rate in Combo versus 4.2% rate in EES (Non-inferiority margin 7%, non-inferiority p-value 0.020)
  • Combo 12-month late loss and binary restenosis were comparable to EES
  • Met superiority in 12-month healthy strut coverage by OCT with 91.6% in Combo versus 74.8% in EES (p-value <0.001)

• Safety
  • No HAMA conversion and no Stent Thrombosis in Combo
  • No unanticipated device-related adverse events

• Manuscript in preparation
Next Steps

HARMOMEE Trial

– “Deep Dives” into sub-set and imaging data sets
– Long-term follow-up out to 5 years

Japan

– Shonin Application
– PMS proposal

US

– Consultation on further trial requirements

HBD
Benefits of Participation in HBD

Overcoming Real Challenges

• Internal organization - Alignment
• Clinical and regulatory objectives - Japan “First” Approach
• Trial approval in Japan and US - Simultaneous
• Site contracting & management - Best Practices
• Regional clinical practice - Protocol and Practice Guidelines
• Safety reporting requirements - Common Procedures
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<th><strong>HARMONEE Trial Organization</strong></th>
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Thank You