Evaluation COMBO’s Healing Profile
The EGO-COMBO Serial OCT Study

OrbusNeich Dual Therapy COMBO Stent Symposium

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Potential conflicts of interest

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(Queen Mary Hospital, University of Hong Kong)

☐ I have the following potential conflicts of interest to report:

☐ Research contracts
☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☒ I do not have any potential conflict of interest to declare

The stents were provided by OrbusNeich as investigational devices.
The Core Laboratory Charges are supported by OrbusNiech.
Genous Healing Approach

Coronary blood flow

CD34 EPC Capture Technology

EPCs circulate in the bloodstream

Immobilized antibodies on the stent surface

EPCs are captured by antibodies

EPCs differentiate into endothelial cells

A mature, functional endothelium is formed

Genous stent strut
Endothelial Progenitor Cell (EPC)

Anti-CD34 Antibody (Clone 561 / Qbend 10)

CD34 Cell Surface Antigen

Stent Outer Surface

EPC Capture Coating

Stephen Lee 2013
Genous EPC Capture Stent

Abluminal Sirolimus

Anti-CD34 EPC Capture Coating

Dual Therapy Combo Stent
PCI objective = purely for achieving revascularization = without complicated issues of

Acute failure
Restenosis
Stent thrombosis
Prolonged DAPT

All current DES = can achieved neointimal suppression

But many DES still show Poor Stent Healing :-
drug cytotoxicity, polymer hypersensitivity, local inflammatory reactions, loss endothelial and vasomotor functions
**REMEDEE Study** (non-inferiority design)

**Single De Novo Native Coronary Artery Lesions**
Reference Vessel Diameter: 2.5-3.5 mm
Lesion Length: < 20 mm

2:1 Randomization

- **COMBO™** Dual Therapy Stent (n=124)
- **TAXUS Liberté®** PES (n=59)

Clinical / MACE

30 Day  9 Mo  1 Yr  2 Yr  3 Yr  4 Yr  5 Yr

9 months angiographic late loss

\[ Combo = 0.39 \pm 0.45\text{mm} \quad Taxus = 0.44 \pm 0.56\text{mm} \quad p=0.55 \]

Haude et al.  JACC Intervention 2013
Stent thrombosis is genuine…

Can we predict & prevent it…. With a novel device ?!!

• Most powerful histological predictor of stent thrombosis = **endothelial coverage**
• Most powerful surrogate indicator of endothelialization = **neointimal coverage**
• Best morphometric predictor of LST = **ratio of uncovered to total stent struts**

_Finn et al. Circulation 2007;115;2435-2441_
OCT 10 micron

IVUS 100 micron

IVUS could never be able to detect early stent coverage

OCT an invaluable tool to detect early stent coverage
The EGO-COMBO Study

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Background: After the first-in-man REMEDEE Study, the dual therapy COMBO Stent (OrbusNeich Medical, FL, USA) was further evaluated for its in-vivo pro-healing benefit and neointimal suppression as a DES in this Study, utilizing a sequential longitudinal OCT follow-up approach.
The EGO-COMBO Study

Methods: In this prospective, single center, first-in-man DES healing profile study, 61 patients treated by COMBO Stent (9 months DAPT) were randomly assigned to 4 monthly groups (2nd to 5th month, in 1:2:2:1 ratio).

OCT was performed sequentially 3 times at baseline PCI, early follow-up in 4 monthly groups (for early stent coverage using 6 stringent Categories; every frame & strut analyzed), and then 9 months (for OCT neointimal analysis; every 5 frames). Patient will be followed up for 2 years. Clinical event adjudication, core lab. QCA & OCT analyses were undertaken by Cardiovascular Research Foundation, NY.
The EGO-COMBO Study

**Procedural Characteristics**

<table>
<thead>
<tr>
<th>Patients Treated</th>
<th>n = 61</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessels treated</td>
<td>n = 74</td>
</tr>
<tr>
<td>COMBO Stents Used</td>
<td>n = 88</td>
</tr>
</tbody>
</table>

**Lesion Location**

<table>
<thead>
<tr>
<th>Location</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>32 (43.2%)</td>
</tr>
<tr>
<td>CIR</td>
<td>16 (21.6%)</td>
</tr>
<tr>
<td>RCA</td>
<td>26 (35.1%)</td>
</tr>
</tbody>
</table>

**ACC/AHA Lesion Class**

<table>
<thead>
<tr>
<th>Class</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>26 (35.1%)</td>
</tr>
<tr>
<td>B1</td>
<td>12 (16.2%)</td>
</tr>
<tr>
<td>B2</td>
<td>30 (40.5%)</td>
</tr>
<tr>
<td>C</td>
<td>6 (8.1%)</td>
</tr>
</tbody>
</table>

**Mean Lesion Length (mm)**

18.37±9.39

**Mean Stent Length (mm)**

23.9±7.62

**Mean Stent Size (mm)**

3.68±0.39

**Pre-procedural RD (mm)**

3.13±0.37

**Pre-procedure MLD (mm)**

1.17±0.35

**Pre-procedure DS%**

61.85±10.17%

**Post-procedural MLD (mm)**

2.89±0.38

**Post-procedural DS%**

7.56±6.89%

**Patient Demographics**

<table>
<thead>
<tr>
<th>Category</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr.)</td>
<td>62.2±11.25</td>
</tr>
<tr>
<td>Sex (M)</td>
<td>47 (77%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>25 (41%)</td>
</tr>
<tr>
<td>DM</td>
<td>20 (33%)</td>
</tr>
<tr>
<td>HT</td>
<td>39 (64%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>41 (67%)</td>
</tr>
<tr>
<td>Previous MI</td>
<td>19 (31%)</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>21 (34%)</td>
</tr>
<tr>
<td>CHF</td>
<td>3 (4.9%)</td>
</tr>
<tr>
<td>DM</td>
<td>20 (33%)</td>
</tr>
</tbody>
</table>

**Pre-procedural RD (mm)**

3.13±0.37

**Pre-procedural MLD (mm)**

1.17±0.35

**Pre-procedure DS%**

61.85±10.17%

**Post-procedural MLD (mm)**

2.89±0.38

**Post-procedural DS%**

7.56±6.89%
The EGO-COMBO Study

Baseline OCT

Proper stent apposition

Degree of early coverage (healing profile)

Guiding appropriate DAPT duration

4 groups (2 to 5 months)
OCT strut coverage

9 months OCT
(late loss NIH)

Little late loss as a DES
Reduced stent thrombosis

Baseline OCT
Distal to proximal

Matching frames
at 90 days follow-up
EGO-Combo Study: Dual Therapy Stent at 90 days
The EGO-COMBO Study

CRF Core Laboratory (Akiko Maehara)

(1) Malapposed Frames
(2) Frames over Side-branches
(3) Properly Apposed Frames

Stringent Classification of Early Strut Coverage

Definitely Uncovered  Uncovered / Fibrin  Partially Uncovered

Uncovered

Covered (corrugated)  Covered (embedded)  Covered (proliferative)
The EGO-COMBO Study

61 patients (33% DM) received 88 COMBO stents. From 2\textsuperscript{nd} to 5\textsuperscript{th} monthly group, the mean covered struts % increased rapidly from 84.3%, 90.2%, 90.5% to 92% (interpolated 100% coverage at around 150 days).
## The EGO-COMBO Study

### EGO-COMBO Angiographic QCA Results

<table>
<thead>
<tr>
<th></th>
<th>Early Follow-Ups</th>
<th>Late FU</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2\textsuperscript{nd} Month (N=12)</td>
<td>3\textsuperscript{rd} Month (N=25)</td>
</tr>
<tr>
<td><strong>MLD (mm)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-stent (mean ± SD)</td>
<td>2.89 ± 0.39</td>
<td>2.88 ± 0.35</td>
</tr>
<tr>
<td>In-segment (mean ±SD)</td>
<td>2.66 ± 0.31</td>
<td>2.64 ± 0.4</td>
</tr>
<tr>
<td><strong>Percent diameter stenosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-stent (mean ± SD)</td>
<td>6.13 ± 4.76</td>
<td>8.25 ± 5.51</td>
</tr>
<tr>
<td>In-segment (mean ± SD)</td>
<td>13.26 ± 5.43</td>
<td>15.94 ± 8.75</td>
</tr>
<tr>
<td><strong>Late lumen loss (mm)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-stent (mean ± SD)</td>
<td>-0.05 ± 0.17</td>
<td>0.04 ± 0.22</td>
</tr>
<tr>
<td>In-segment (mean ± SD)</td>
<td>-0.16 ± 0.23</td>
<td>0.02 ± 0.24</td>
</tr>
</tbody>
</table>

* N = number of vessels treated in each monthly group.
The EGO-COMBO Study

Results:

At 9 months, the mean OCT neointimal thickness by CRF Core Lab. was 0.157mm and area 1.445mm$^2$, with a corresponding QCA late loss of 0.24mm.

At 9 months FU, 1 patient had non-ischemic angiographic stenosis treated by simple ballooning; otherwise no other MACE (restenosis nor stent thrombosis) was recorded to date, totalling a MACE rate of only 1.64% (1/61) throughout a mean FU period of 19 months.
Sequential longitudinal OCT FU with a very stringent strut coverage classification

OCT should be adopted as a vigorous & novel step for guiding any new stent platform.

- Baseline OCT
- 4 to 5 groups (2 to 5 months) OCT strut coverage
- 9 to 12 months OCT (late loss NIH)

Proper stent apposition

Degree of early coverage (healing profile)

Guiding appropriate DAPT duration

Little late loss as a DES

Reduced stent thrombosis

Very stringent strut coverage classification

May predict / prevent late stent thrombosis, rather than waiting for years to observe for adverse effects.

Dual Therapy COMBO Stent: could be a Novel Device
The EGO-COMBO Study (long term follow-up)

Study Case 47:
Admitted on 18 months for ACS.
Unstable plaque RCA treated by PTCS.
COMBO stent on LAD re-examined.

<table>
<thead>
<tr>
<th></th>
<th>Pre-PCI</th>
<th>Post-PCI</th>
<th>4 Months</th>
<th>9 Months</th>
<th>18 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>RD (mm)</td>
<td>2.53</td>
<td>2.57</td>
<td>2.47</td>
<td>2.49</td>
<td>2.42</td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>1.1</td>
<td>2.35</td>
<td>2.27</td>
<td>2.2</td>
<td>2.18</td>
</tr>
<tr>
<td>Late Loss (mm)</td>
<td>0.08</td>
<td>0.15</td>
<td>0.17</td>
<td>0.133</td>
<td>0.17</td>
</tr>
<tr>
<td>OCT NIT (mm)</td>
<td>0.070</td>
<td>0.147</td>
<td>0.133</td>
<td>0.133</td>
<td>0.133</td>
</tr>
<tr>
<td>OCT NIA (mm²)</td>
<td>0.610</td>
<td>1.154</td>
<td>1.079</td>
<td>1.079</td>
<td>1.079</td>
</tr>
</tbody>
</table>
Interim Results from 9M to 24M (26 patients)

**QCA Δ Neointimal Thickness** $0.07 \pm 0.13mm$ ($p=ns$)

**OCT NIT / NIA** pending Core Lab analysis.

Apart from full healing (100% coverage), also **durable results as a DES with NO late loss catch up.**
All patients had 100% coverage by 9 months FU with durable outcomes at 24 months:
- all 60 patients remain ASYMPTOMATIC (MACE remains at 1.6%).
- none has stent thrombosis (as predicted by the healing profile curve).

So far 29 patients due for 24 months FU restudied by angiogram and OCT:
- no late catch-up; no thrombus; mild NIT; no neo-atherosclerosis, no “sun-flowering”.

**Same patient**
2 lesions on LAD
24M Combo Proximal
22M Cypher Distal
Conclusion: The dual therapy COMBO stent is the first DES with a healing profile established (rapid healing and strut coverage). Its promising outcomes appeared to support the benefits of the dual therapy approach, with minimal restenosis (only in 1 case) as a DES, and without late stent thrombosis or late loss catch up after 24 months of FU.

*Future new stent platforms should be tested using this approach with vigorous sequential longitudinal OCT examination.*