Randomized Trial of COBRA PzF Stenting to REDUCE Duration of Triple Therapy (COBRA-REDUCE)

Robert A. Byrne, MB BCh PhD

on behalf of the COBRA-REDUCE Investigators

Clinical Trial Registration: NCT02594501
Personal fees

- None

Research funding

- Research contract with institution of prior employment: CeloNova Biosciences
COBRA PzF™ NanoCoated Coronary Stent (NCS)

**Polyzene-F**
Poly [bis (trifluoroethoxy) phosphazene]

- High molecular weight ultra pure polyphosphazene
- Stable fluorinated polymer, does not degrade under biological condition
- Thrombo-resistant, non inflammatory and pro-healing in pre-clinical studies

**Strut Material:** Cobalt Chromium Alloy

**Strut Thickness:** 71 μm

**NanoCoating:** Polyzene -F

**Polyzene-F Thickness:** ≤0.05 μm
**COBRA-REDUCE | Trial Overview**

**Design**

- Randomized, open-label, active-controlled, assessor-blinded, multi-center trial

**OBJECTIVE** To determine whether COBRA PzF Stent with short duration DAPT (14d) results in a lower incidence of bleeding without increasing thrombotic events compared with DES * with std DAPT (3-6m) in patients taking OAC §

**PRINCIPAL INVESTIGATORS**

Adnan Kastrati (PI), Deutsches Herzzentrum München, Technische Universität, Munich, Germany

Robert A. Byrne (Co-PI), Mater Private Hospital, RCSI University, Dublin, Ireland

Clinical Trial Registration: NCT02594501

- 996 patients enrolled between Feb 2016 and May 2020 in 59 sites in Europe & USA

**Treatment Group** (N=495)
- Received COBRA stent only (N=481)
- Clinical follow-up at 6 months in 97.6% (N=483)

**Control Group** (N=501)
- Received DES only (N=499)
- Clinical follow-up at 6 months in 96.6% (N=484)

Withdrew consent 1
Lost to FU 2
FU incomplete 9

Withdrew consent 6
Lost to FU 5
FU incomplete 6

*FDA-approved second-generation DES

§OAC dose intensity reduction permitted at PI’s discretion
OAC dose-reduction was permitted at discretion of PI.

**CONTROL DEVICE:** FDA-approved DES

**TREATMENT DEVICE:** COBRA stent
COBRA-REDUCE: Trial Organization

- US: 370
- EU: 626
COBRA-REDUCE | Primary Endpoint
BARC 2-5 Bleeding after 14 days*

<table>
<thead>
<tr>
<th>COBRA + 14d DAPT</th>
<th>DES + 3-6m DAPT</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>COBRA + Short DAPT</td>
<td>DES + Std DAPT</td>
<td>0.477</td>
</tr>
<tr>
<td>7.5% (35/466)</td>
<td>8.9% (42/474)</td>
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</tr>
</tbody>
</table>
COBRA-REDUCE | Co-Primary Endpoint Thrombotic Composite

Composite of Death/MI/Stent Thrombosis/Ischemic Stroke

<table>
<thead>
<tr>
<th></th>
<th>COBRA + 14d DAPT</th>
<th>DES + 3-6m DAPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>COBRA + Short DAPT</td>
<td>7.7%</td>
<td>5.2%</td>
</tr>
<tr>
<td>Difference +2.5% (95% CI 5.15%)</td>
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</tbody>
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Difference +2.5% (95% CI 5.15%)
Secondary bleeding endpoints

- **BARC 3-5 (after 14 d)**
  - COBRA + short DAPT: 3.9%
  - DES + standard DAPT: 4.2%
  - P = 0.869*

- **BARC 3-5 (after randomization)**
  - COBRA + short DAPT: 6.8%
  - DES + standard DAPT: 6.1%
  - P = 0.693*

- **BARC 2-5 (after randomization)**
  - COBRA + short DAPT: 11.7%
  - DES + standard DAPT: 14.4%
  - P = 0.212*

- **BARC 1-5 (after randomization)**
  - COBRA + short DAPT: 13%
  - DES + standard DAPT: 18.3%
  - P = 0.026*

*superiority analysis
### Secondary thrombo-embolic endpoints

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>COBRA + short DAPT</th>
<th>DES + standard DAPT</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>4.1</td>
<td>2.9</td>
<td>0.383*</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>2.3</td>
<td>1.5</td>
<td>0.354*</td>
</tr>
<tr>
<td>MI</td>
<td>2.8</td>
<td>1.7</td>
<td>0.279*</td>
</tr>
<tr>
<td>Def/prob ST</td>
<td>0.6</td>
<td>0.6</td>
<td>&gt;0.99*</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>1.3</td>
<td>0.9</td>
<td>0.545*</td>
</tr>
<tr>
<td>ID-TLR</td>
<td>3.7</td>
<td>0.9</td>
<td>0.004*</td>
</tr>
</tbody>
</table>

*superiority analysis*
In patients undergoing PCI for acute or chronic coronary syndromes who are receiving oral anticoagulation, stenting with Cobra PzF stents with 14 days DAPT with or without reduced intensity OAC did not reduce bleeding and did not meet non-inferiority criteria with respect to thrombotic events compared with standard DES and 3-6 months of DAPT.
Treatment with Cobra PzF stent was safe with ST rates considerably lower than those seen in earlier trials with HBR patients despite DAPT duration of only 14 days.

Ongoing follow-up and planned analysis of secondary outcomes at 12 months is awaited in order to assess comparative efficacy of the treatment arms in relation to the study devices.

Analyses of bleeding events according to medication compliance, OAC dose and number of ARC-HBR criteria will permit examination of interaction between treatment effect, anticoagulation intensity and baseline bleeding risk.