KEY CLINICAL FINDINGS FROM THE ILUMIEN TRIAL SERIES

Past

**CLI-OPCI**
OCT improves outcomes vs. angiography

**OPUS-Class Study**
Reliability of OCT measurement vs. IVUS and angiography

**OCT Safety and Efficacy**
Non-occlusive OCT study

Present–2015

**ILUMIEN I**
Define and evaluate OCT stent guidance parameters and determine impact on physician decision making

**ILUMIEN II**
OCT vs. IVUS comparison of stent expansion

**ILUMIEN III**
OCT/IVUS/Angio prospective randomized trial

Future

**ILUMIEN IV**
Randomized controlled outcomes, under development

Other areas under consideration
- Bifurcation
- BVS
- ACS

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Highlights .................. 4
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St. Jude Medical
CLINICAL HIGHLIGHTS FROM ILUMIEN I

#1 OCT impacted PCI procedures in 65% of patients either pre-PCI and/or post-PCI.

- Pre-PCI Change
  - Stent Length
    - Longer 43%
    - Shorter 25%
  - Stent Diameter
    - Larger 8%
    - Smaller 31%

- Post-PCI Change
  - 27%
  - Resulted in reduction of:
    - Malapposition from 51% to 19%
    - Malapposition + Edge Dissection from 16% to 5%

#2 Use of OCT guidance pre- and post-PCI was associated with reduced rates of MI.

- No Pre-PCI Change, or Post-PCI Optimization, Based on OCT (n = 137)
  - 1-Year MI (ARC) 12.1%

- OCT-Driven Pre-PCI Change and Post-PCI Optimization Made (n = 65)
  - 0%

References Brief Summary

While this is early data and it needs to be confirmed, these studies validate the important contribution of OCT in PCI treatment planning, and show a correlation between OCT imaging guidance and improved patient outcomes.
**ILUMIEN I CLINICAL DATA**

**OVERVIEW**

**Title:** ILUMIEN I - Observation Study to Assess the Additive Role of OCT to FFR and Angiography in Optimizing the Outcome in Patients Undergoing PCI for Both Stable and Acute Ischemic Syndromes

**ID:** NCT01663896

**Sponsor:** St. Jude Medical

**Purpose:** To define and evaluate OCT stent guidance parameters through prospective data collection in PCI procedures of de novo lesions

**PRIMARY OBJECTIVE:**
- Identify OCT peri-procedural guidance parameter(s) for stent implantation

**SECONDARY OBJECTIVES:**
1. Assessment of impact of OCT on physician decision making pre- and post-PCI
2. Correlation/relationship of OCT parameters, as defined by OCT volumetric analysis, on pre- and post-intervention FFR values
3. Consideration of health economics data and resource utilization

**EXCLUSION:**
- Subjects with target left main lesion, subjects with restenosis or stent thrombosis in target vessel; aorto-ostial lesion location within 3 mm of aorta junction (both right and left); extreme angulation (>90°) or excessive tortuosity (> two 45° angles) proximal to or within target lesion; vessel(s) and lesion(s) not amenable for PCI, i.e., diffuse disease.

**INCLUSION CRITERIA:**
- De novo coronary artery disease in target vessel; single or multi-vessel disease (max 3 lesions in 2 vessels, max 2 lesions/vessel); angiographically significant (> 50% visual estimation) stenosis

**PUBLICATION:**
- Presented at EuroPCR 2015 by William Wijns MD, PhD
  - Cardiovascular Research Center, OLV Hospital, Aalst, Belgium on behalf of the Global ILUMIEN I investigators

**POST-OCT PCI FINDINGS AND OPTIMIZATION:**
- Abnormal OCT findings are common after “successful” PCI: malapposition (32%), edge dissection (32%), underexpansion (27%), malapposition + edge dissection (9%), tissue or thrombus protrusion (4%).

**SUMMARY AND CONCLUSIONS:**
- Physician decision making was influenced by OCT findings either pre-PCI and/or post-PCI in 65% of patients, mostly in patients with more complex disease.

**MACE events were rare, including stent thrombosis, up to 1 year follow-up. Change in strategy based on pre- and post-PCI OCT findings appears to be associated with reduced rates of peri-procedural myocardial infarction (post-hoc analysis). This hypothesis-generating observation should be tested prospectively and inform the design of future randomized trials.

**POST-OCT PCI FINDINGS AND OPTIMIZATION:**
- Abnormal OCT findings are common after “successful” PCI: malapposition (32%), edge dissection (32%), underexpansion (27%), malapposition + edge dissection (9%), tissue or thrombus protrusion (4%).
- Abnormalities identified by OCT deemed unsatisfactory by operators were malapposition (14.5%), stent underexpansion (7.6%), edge dissection (2.7%).
- Further optimization significantly reduced rates of malapposition from 51% to 19% (p = 0.01) and rates of malapposition + edge dissection from 18% to 5% (p = 0.05).

**SUMMARY AND CONCLUSIONS:**
- Physician decision making was influenced by OCT findings either pre-PCI and/or post-PCI in 65% of patients, mostly in patients with more complex disease.
- MACE events were rare, including stent thrombosis, up to 1 year follow-up. Change in strategy based on pre- and post-PCI OCT findings appears to be associated with reduced rates of peri-procedural myocardial infarction (post-hoc analysis). This hypothesis-generating observation should be tested prospectively and inform the design of future randomized trials.
- Further analysis of OCT guidance parameters that predict clinical outcomes at 1 year is ongoing.
CLINICAL HIGHLIGHTS FROM ILUMIEN II

#1 OCT’s ability to achieve superior resolution compared to IVUS allows for perfection of PCI.

#2 Stent expansion was comparable between OCT and IVUS.

These findings are important and show similar procedural outcomes and are being investigated to demonstrate those translate to patient outcomes.
ILUMIEN II CLINICAL DATA

OVERVIEW

**TITLE:** ILUMIEN II - A Retrospective Evaluation of Stent Expansion with OCT Guidance vs. IVUS Guidance

**SPONSOR:** St. Jude Medical (ILUMIEN I and II)

**OBJECTIVE:** To compare the degree of stent expansion achieved after OCT guidance to that achieved with IVUS guidance

**PUBLICATION:** Presented at EuroPCR 2015 by Gregg W. Stone, MD

**PRIMARY ENDPOINT:** Post-PCI stent expansion (%) defined as the minimum stent area (MSA) divided by the mean reference lumen area. Assessed by OCT in ILUMIEN I and by IVUS in ADAPT-DES

**SECONDARY ENDPOINTS:**
1. IVUS and OCT core lab measures:
   - Mean stent expansion (volume/length) divided by mean reference lumen area
   - Prevalence of major edge dissection (≥ 3 mm in length)
   - Prevalence of major stent malapposition (malapposition distance/luminal diameter ≥ 20%)
2. Angiographic core lab measures (independent of technique). Post-PCI MLD, mean lumen diameter, %DS and acute gain

ILUMIEN II STUDY DESIGN

Retrospective comparison of OCT guidance in ILUMIEN I and IVUS guidance in ADAPT-DES

KEY DATA


**TABLE 1. Pre-PCI QCA (Matching parameter)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OCT (n = 286)</th>
<th>IVUS (n = 286)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcification (moderate or severe)*</td>
<td>60 (21.0%)</td>
<td>56 (19.6%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Thrombus</td>
<td>8 (2.8%)</td>
<td>7 (0.8%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Bifurcation</td>
<td>97 (33.9%)</td>
<td>93 (32.5%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Apical Stenosis (moderate or severe)</td>
<td>21 (7.3%)</td>
<td>23 (8.0%)</td>
<td>0.75</td>
</tr>
<tr>
<td>Tortuosity (moderate or severe)</td>
<td>21 (7.8%)</td>
<td>23 (8.0%)</td>
<td>0.75</td>
</tr>
<tr>
<td>TIMI-3 Flow</td>
<td>257 (89.9%)</td>
<td>255 (89.2%)</td>
<td>0.78</td>
</tr>
<tr>
<td>RVD, mm*</td>
<td>2.7 (2.3, 3.0)</td>
<td>2.7 (2.4, 3.0)</td>
<td>0.17</td>
</tr>
<tr>
<td>MLD, mm</td>
<td>2.7 (2.4, 3.0)</td>
<td>2.7 (2.4, 3.0)</td>
<td>0.54</td>
</tr>
<tr>
<td>Diameter Stenosis, %</td>
<td>64.3 (57.0, 72.1)</td>
<td>64.0 (56.9, 75.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>Lesion Length, mm*</td>
<td>14.9 (10.8, 21.3)</td>
<td>14.1 (9.8, 23.5)</td>
<td>0.54</td>
</tr>
</tbody>
</table>

**TABLE 2. Post-PCI QCA**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OCT (n = 286)</th>
<th>IVUS (n = 286)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVD, mm*</td>
<td>2.6 (2.3, 2.9)</td>
<td>2.7 (2.4, 3.0)</td>
<td>0.12</td>
</tr>
<tr>
<td>In-stent Measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MLD, mm</td>
<td>2.5 (2.3, 2.9)</td>
<td>2.6 (2.3, 2.8)</td>
<td>0.78</td>
</tr>
<tr>
<td>Mean Ld, mm</td>
<td>2.9 (2.6, 3.2)</td>
<td>2.9 (2.7, 3.2)</td>
<td>0.76</td>
</tr>
<tr>
<td>Acute Gain, mm</td>
<td>1.6 (1.3, 1.9)</td>
<td>1.6 (1.4, 1.9)</td>
<td>0.60</td>
</tr>
<tr>
<td>Diameter Stenosis, %</td>
<td>6.3 (2.8, 9.6)</td>
<td>6.4 (2.9, 11.9)</td>
<td>0.07</td>
</tr>
<tr>
<td>In-segment Measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MLD, mm</td>
<td>2.2 (2.0, 2.6)</td>
<td>2.3 (2.1, 2.6)</td>
<td>0.01</td>
</tr>
<tr>
<td>Acute Gain, mm</td>
<td>1.3 (1.0, 1.6)</td>
<td>1.4 (1.1, 1.7)</td>
<td>0.005</td>
</tr>
<tr>
<td>Diameter Stenosis, %</td>
<td>13.0 (9.6, 19.8)</td>
<td>12.3 (9.8, 17.4)</td>
<td>0.07</td>
</tr>
<tr>
<td>Proximal Stent Edge MLD, mm</td>
<td>2.8 (2.5, 3.2)</td>
<td>2.8 (2.5, 3.2)</td>
<td>0.046</td>
</tr>
<tr>
<td>Distal Stent Edge MLD, mm</td>
<td>2.3 (2.0, 2.6)</td>
<td>2.4 (2.1, 2.8)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**TABLE 3. Multi-variable Analysis: Entire Study Population (n = 940)**

<table>
<thead>
<tr>
<th>Analysis</th>
<th>OCT (n = 264)</th>
<th>IVUS (n = 260)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent Expansion (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Stent Expansion (%)</td>
<td>72.6</td>
<td>79.4</td>
<td>0.007</td>
</tr>
<tr>
<td>QCA DS In-stent (%)</td>
<td>69.6</td>
<td>74.8</td>
<td>0.007</td>
</tr>
<tr>
<td>QCA DS In-segment (%)</td>
<td>62.1</td>
<td>67.1</td>
<td>0.007</td>
</tr>
<tr>
<td>Adjusted P-values</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OCT vs. IVUS guidance</td>
<td>0.84</td>
<td>0.30</td>
<td>0.19</td>
</tr>
<tr>
<td>Age</td>
<td>0.04</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Prior Myocardial Infarction</td>
<td>*</td>
<td>0.04</td>
<td>*</td>
</tr>
<tr>
<td>Lesion Length</td>
<td>&lt; 0.0001</td>
<td>0.0009</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Reference Vessel Diameter</td>
<td>0.011</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Bifurcation</td>
<td>0.0066</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Tortuosity (moderate or severe)</td>
<td>0.01</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Calcification (moderate or severe)</td>
<td>0.007</td>
<td>*</td>
<td>0.002</td>
</tr>
<tr>
<td>LAD Location</td>
<td>*</td>
<td>0.02</td>
<td>*</td>
</tr>
<tr>
<td>Reference Availability</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>*</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- In the present comparison of patients undergoing OCT-guided stenting from ILUMIEN I and IVUS-guided stenting from ADAPT-DES, OCT guidance was associated with comparable stent expansion, slightly greater in-segment %DS, and similar rates of major stent malapposition, tissue protrusion and stent edge dissection as IVUS guidance.

- The results of angiography-guided, IVUS-guided and OCT-guided stent implantation are currently being evaluated in the prospective, multi-center, randomized ILUMIEN III: OPTIMIZE PCI trial.
ILUMIEN III TRIAL DESIGN

PROSPECTIVE, POST-MARKET, INTERNATIONAL, MULTI-CENTER, RANDOMIZED TRIAL

OVERVIEW

TITLE: ILUMIEN III: OPTIMIZE PCI
Optical Coherence Tomography (OCT) Compared to Intravascular Ultrasound (IVUS) and Angiography to Guide Coronary Stent Implantation: a Multi-center Randomized Trial in PCI
a.k.a. Stent Guidance by OCT vs. IVUS and vs. Angiography

TYPE: Prospective, post-market, international, multi-center, randomized trial

PERIOD: Q2 2015 - Q2 2017

DEVICES: ILUMIEN™ OPTIS™ PCI Optimization System and OPTIS™ Integrated System for OCT, and available IVUS System

SPONSOR: St. Jude Medical

ARO: Cardiovascular Research Foundation (CRF), New York

Centers: Approximately 35 sites in the United States and outside the United States; approximately 25% of subjects will be enrolled in the United States

OBJECTIVE: To demonstrate the safety and efficacy of an OCT-guided strategy for stent implantation

PRIMARY ENDPOINTS:

1. Non-inferiority of OCT-guided stenting to IVUS-guided stenting
2. Superiority of OCT-guided stenting to Angiography-guided stenting
3. Superiority of OCT-guided stenting to IVUS-guided stenting

Primary Efficacy Endpoint (powered): Post-PCI MSA assessed by OCT in each randomized arm, measured at the independent OCT core laboratory blinded to imaging modality assignment. Testing will be done in a hierarchical manner as follows:

RANDOMIZED 1:1:1, STRATIFIED BY SITE

Patients undergoing coronary angiography with possibility of PCI will be consented to participate in the study.

Sites will declare to the SJM electronic randomization system the CASS segment of the study lesion. In general this should be the most proximal lesion supplying the largest amount of myocardium. Note: The target vessel may contain only one target lesion and only one lesion may be randomized. A single lesion is defined as a segment of the coronary artery that has angiographically evident narrowing(s), without any intervening normal segment longer than 10 mm. The total length of stenting shall not exceed 50 mm.

Patients undergo PCI with:

1. OCT Guidance
2. IVUS Guidance
3. Angiography Guidance

Baseline and post-PCI imaging with their randomized modality

Blinded post-PCI OCT performed to allow comparison of OCT derived MSA in all groups

After hospital discharge, 30-Day follow-up (±7 days, office visit or phone call)

1-Year follow-up (±30 days, office visit or phone call)

INCLUSION CRITERIA:

1. Patient with an indication for PCI including:
   - Angina (stable or unstable)
   - Silent ischemia (a visually estimated target lesion diameter stenosis of ≥ 70%, a positive non-invasive stress test, or FFR ≤ 0.80 must be present)
   - NSTEMI, or
   - Recent STEMI (> 24 hours from initial presentation and stable)
2. Patients will undergo cardiac catheterization and possible or definite PCI with intent to stent using any non-investigational metallic drug-eluting stent (DES)
3. The target lesion must be located in a native coronary artery with visually estimated reference vessel diameter of ≥ 2.25 mm to ≤ 3.50 mm
4. Lesion length < 40 mm

EXCLUSION CRITERIA:

1. Presence of one or more comorbidities that reduces life expectancy to less than 12 months or may interfere with protocol study processes
2. The presence of any non-study lesion in the target vessel with angiographic diameter stenosis > 50%, or any additional target vessel stenosis that requires PCI either during or within 12 months after the study procedure
3. Left main diameter stenosis ≥ 30% or left main PCI planned
4. Ostial RCA study target lesion
5. Chronic total occlusion (TIMI flow 0/1) study target lesion
6. Bifurcation study lesion with a planned dual-stent strategy
7. In-stent restenosis study target lesion

STUDY CHAIR AND PRINCIPAL INVESTIGATOR

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Columbia University Medical Center, NYC

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References

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