Current & Future Stent Design for Drug-eluting Stent
– Focused on the Updated Resolute Program –

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1. Endeavor Resolute vs. Resolute Integrity

2. Brief Summary of Recent Clinical Data
   1) Data from TCT 2010
   2) Data from ACC 2011
Unique Manufacturing Process

- Resolute Integrity DES uses Continuous Sinusoid Technology, a unique manufacturing process pioneered by Medtronic.
  - Continuous Sinusoid Technology uses a single continuous piece of wire that is formed into the sinusoidal shape.
  - It is then wrapped around a mandrel to give the cylindrical shape of the stent.
  - The stent is then fused in strategic locations to ensure optimum flexibility, conformability and strength.
Conventional Laser Cut Stent Manufacturing
Integrity Continuous Sinusoidal Technology
Why is Resolute Integrity DES More Deliverable?

Fluid Range of Motion

CONVENTIONAL LASER CUT STENTS

Separate stiff segments connected by flexible connectors limit range of motion

- Horizontally
- Vertically

CONTINUOUS SINUSOID

Continuous sinusoid technology will flex continually

- Horizontally
- Vertically
- Rotationally

⇒ Fluid range of motion for streamlined delivery in 3D anatomy.
Fluid Range of Motion

*Integrity stent platform provides continuous range of motion.*

DES:

- Promus Element
- Xience Prime
- Resolute Integrity

Separate stiff segments in laser cut stents limit the range of motion.

The helical design of Integrity continually flexes.
Similarities in Cell Design, Stent Pattern & Scaffolding
Coating Layer Comparison – Resolute DES vs. Resolute Integrity DES

<table>
<thead>
<tr>
<th>Coating Composition</th>
<th>Resolute DES</th>
<th>Resolute Integrity DES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primer: Parylene</td>
<td>SAME</td>
<td>SAME</td>
</tr>
<tr>
<td>35% Zotarolimus</td>
<td>SAME</td>
<td>SAME</td>
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<tr>
<td>65% BioLinx</td>
<td>SAME</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Dose Density</th>
<th>~1.6 µg/mm²</th>
<th>~1.6 µg/mm²</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Coating Thickness</th>
<th>SAME</th>
<th>SAME</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 µm</td>
<td>6 µm</td>
<td>6 µm</td>
</tr>
<tr>
<td>91 µm</td>
<td>91 µm</td>
<td>91 µm</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strut Dimensions</th>
<th>SAME</th>
<th>SAME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent strut</td>
<td>Stent strut</td>
<td>Stent strut</td>
</tr>
</tbody>
</table>
Drug Load Comparison

Resolute Integrity DES has ~.9 mm helical wraps with nominal dose density of ~1.6 µg/mm²

Resolute DES has 1.0mm segments with nominal dose density of ~1.6 µg/mm²

Resolute Integrity DES

Resolute DES

Total drug load is identical for both stents

Example based on medium vessel 18 mm length stent
In-Vivo Drug Delivery: Resolute DES vs Resolute Integrity DES

In-Vivo Elution: Comparison of Resolute DES and Resolute Integrity DES through Day 60

In-Vivo Bioequivalence Testing: Comparison of Resolute DES and Resolute Integrity DES

- EQUIVALENT in-vivo drug release profile
- EQUIVALENT zotarolimus arterial tissue level
- EQUIVALENT blood drug levels

⇒ In-Vivo Bioequivalence Testing demonstrated equivalent drug delivery characteristics between Resolute DES and Resolute Integrity DES.
MicroTrac Delivery System Enhances Capabilities

**Improvements**
- Increased Shaft Column Strength
- Extended Hydrophilic Coating
- Reduced Profile Exchange Joint
- Reduced Under Stent Catheter Profile

**Performance Gains**
- Enhanced push force & efficiency
- Smoother Tracking
- 6F KBT Compatibility
- Smaller Crossing Profiles

**Clinical Benefits**
- Ease crossing calcifications
- Facilitate navigating distal tortuous anatomies
- Excellent kissing balloon technique performance
- Improve crossing narrow lesions

MicroTrac delivery system enhances device performance.
Trackability

- Trackability assesses the amount of effort required to track a DES through a 3-dimensional tortuous path.
- Challenging curvature differentiates stent designs.

Resolute Integrity DES is significantly more trackable.

Bench test data vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES on file at Medtronic, Inc. These tests may not be indicative of clinical performance.
Crossing Profile

- The smaller a DES’s crossing profile, the better able it is to cross through narrow stenoses.

<table>
<thead>
<tr>
<th>DES</th>
<th>Stent Crossing Profile, 2.5 mm (mm)</th>
<th>Stent Crossing Profile, 3.5 mm (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resolute Integrity</td>
<td>1.01(0.039”)</td>
<td>1.17(0.046”)</td>
</tr>
<tr>
<td>Promus Element</td>
<td>1.01</td>
<td>1.17</td>
</tr>
<tr>
<td>Xience Prime</td>
<td>1.05</td>
<td>1.24</td>
</tr>
</tbody>
</table>

Resolute Integrity DES has an excellent crossing profile.

Bench test data vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES on file at Medtronic, Inc. These tests may not be indicative of clinical performance.
Pushability

- Pushability measures the ability to transfer force applied by the operator at the proximal end of the catheter to the distal end.
- With greater push efficiency, the Resolute Integrity system may ease the crossing of narrow and/or calcified lesions.

⇒ Resolute Integrity DES is significantly more pushable.

Bench test data vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES on file at Medtronic, Inc. These tests may not be indicative of clinical performance.
Lesion Access
Blinded Physician Assessment of Deliverability

- Physicians rated Resolute Integrity DES significantly higher than Xience Prime DES and Promus Element DES in both small and medium vessels sizes.

Resolute Integrity DES significantly outperformed competition in blinded in-vivo studies.
Placement Accuracy: Radiopacity

Physician Assessed Radiopacity in In-vivo Animal Studies

RADIOPACITY
Promus Element DES was most radiopaque, followed by Resolute Integrity DES, then Xience Prime DES. Promus Element DES uses platinum enriched alloy material that increases radiopacity.

TRADEOFFS
Promus Element DES alloy material does have tradeoffs:
• Unknown strength and fatigue resistance
• New alloy with no prior history of human use

RESOLUTE INTEGRITY DES vs Xience Prime DES and Resolute DES
Radiopacity of Resolute Integrity DES is better than Xience Prime DES.
Radiopacity was also assessed against Resolute DES and determined to be similar; Resolute DES & Resolute Integrity DES have similar strut thicknesses and surface area.

⇒ Resolute Integrity DES has better radiopacity than Xience Prime DES.

Test data on file at Medtronic, Inc.
These tests may not be indicative of clinical performance.
Lesion Coverage

Radial Strength

- Radial strength is the ability of the stent to resist external forces and maintain its diameter.

⇒ Resolute Integrity DES has excellent radial strength.

Bench test data vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES on file at Medtronic, Inc. These tests may not be indicative of clinical performance.
Conformability Case Study

• A conformable stent will provide excellent strut apposition to the vessel wall while minimizing vessel straightening.

• Conformability Challenge:
  – Physician Assessment
  – Prof. Stephen WL Lee, Queen Mary Hospital, Hong Kong.

• Case, 3 November 2009:
  – Proximal RCA
    • Very severe tortuosity
    • Severe calcification
    • Type C lesion
    • 80% stenosis

⇒ Resolute Integrity DES is highly conformable.
Excellent Side Branch Access

- A maximum cell perimeter will allow you to address a wide range of side branch diameters and angulations.
- Resolute Integrity DES’s round struts facilitate wire access and balloon and stent crossing into a side branch.

Resolute Integrity DES provides excellent side branch access.

Bench test data vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES on file at Medtronic, Inc. These tests may not be indicative of clinical performance.
Resolute Integrity DES Expanded Size Matrix

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>Stent Length (mm)</th>
<th>22</th>
<th>26</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.25</td>
<td>8 12 14 18</td>
<td>22</td>
<td>26</td>
<td>30</td>
</tr>
<tr>
<td>2.50</td>
<td>8 12 14 18</td>
<td>22</td>
<td>26</td>
<td>30</td>
</tr>
<tr>
<td>2.75</td>
<td>8 12 14 18</td>
<td>22</td>
<td>26</td>
<td>30</td>
</tr>
<tr>
<td>3.00</td>
<td>9 12 15 18</td>
<td>22</td>
<td>26</td>
<td>30 34 38</td>
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<tr>
<td>3.50</td>
<td>9 12 15 18</td>
<td>22</td>
<td>26</td>
<td>30 34 38</td>
</tr>
<tr>
<td>4.00</td>
<td>9 12 15 18</td>
<td>22</td>
<td>26</td>
<td>30 34 38</td>
</tr>
</tbody>
</table>

22-mm and 26-mm lengths expand the size matrix and replace the 24-mm Resolute DES stent length.

- Resolute Integrity DES adds 3 new lengths to the size matrix, expanding product offering from 39 sizes to 48 sizes.

⇒More even spacing and additional longer lengths allow more optimal lesion matching.
Overview of Packaging Improvements

• Only DES among market leaders to have a single pouch package.
• A single pouch configuration simplifies access to product in a sterile field, especially when time is a critical factor.
• A smaller box facilitates product handling and frees up more shelf space in the stock room.
Summary; Make the Complex Simple

Resolute Integrity offers you:
- Superior deliverability\(^1\) without compromise.
- Identical drug delivery characteristics to a platform proven for complex daily practice.
- Powerful DES therapy made even easier to deliver to complex lesions.
- Latest in DES innovation that redefines performance.
- Designed for the needs of an increasingly complex clinical practice.

The Resolute Integrity stent system will help you navigate tortuous anatomies and deliver powerful efficacy, making it easier for you to address the needs of your complex cases.

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\(^1\)Bench test data vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES on file at Medtronic, Inc. These tests may not be indicative of clinical performance. RESOLUTE All Comers 12-month data. Case conducted using Integrity BMS.
I am one of known CTO guy...

1. CTO PCI Expert & Preceptorship
2. Director in Scientific Committee
3. CTO live in many hospitals...
COURSE OVERVIEW

- Instructor: Dr. Kha Seung Woon
- Technical Improvement in Complex Coronary & Peripheral Intervention
- Clinical Research in Cardiovascular Field

REGISTRATION

Personal Information

Name
Hospital & Specialty
E-mail address
Telephone/Mobile

Areas of Interests

- How to get out of trouble (procedural complication)
- How to get access in difficult CTO Case
- Current treatment strategies and device selection
- Clinical Research in Cardiovascular Field
Korean Visiting Professors

Prof. Park SH & Cho YH’s Live
Visiting Professor 2011; Young & Ambitious Drs
Never Give Up & Until Happy Ending
Korean Visiting Professors; Happy Endings!!
Strong New Data from TCT 2010

• Strong Performance in More All Comer Patients
  – RESOLUTE International 12-month results

• Valuable Evidence in Complex Patient Subgroups
  – RESOLUTE All Comers 12-month subgroup results

• Strong Results in the Long-Term
  – RESOLUTE 4-yr results

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for complex patient subgroup analysis.
RESOLUTE International

Prospective, Multicenter, Real World Study


All patients with symptomatic coronary artery disease eligible for DES implantation (no lesion/vessel limitations)

Resolute Stent
N = 2200

88 sites International
No angiographic follow-up
25% randomly assigned to 100% monitoring

Clinical endpoints

Primary Endpoint: Composite of Cardiac Death & Target Vessel MI at 12mo
Key Secondary Endpoint: ARC Definite and Probable Stent Thrombosis at 12mo
Drug Therapy: ASA and clopidogrel/ticlopidine ≥ 6mo (per guidelines)

Belardi J. TCT 2010
### Inclusion Criteria

- Coronary artery disease
  - Stable angina
  - Silent ischemia
  - Acute coronary syndrome including UA, NSTEMI and STEMI
- Intention to electively implant at least one Resolute stent
- Lesion characteristics
  - Number of lesions: no limitation
  - Number of vessels: no limitation
  - Lesion length: no limitation
- Written informed consent

### Exclusion Criteria

- Pregnancy
- Inability to comply with follow-up requirements
- Participation in another trial

Belardi J. TCT 2010
RESOLUTE International

Patient Follow-up

2349 Patients Enrolled

30 Day Clinical Follow-up
n = 2342
99.7%

6 Month Clinical Follow-up
n = 2332
99.3%

12 Month Clinical Follow-up
n = 2287
97.4%

Belardi J. TCT 2010
Complex patient definition: bifurcation, bypass grafts, ISR, AMI <72 hr, LVEF <30%, unprotected LM, >2 vessels stented, renal insufficiency or failure (creatinine >140 µmol/L), lesion length >27 mm, >1 lesion per vessel, lesion with thrombus or TO (preprocedure TIMI = 0). With the exception of long lesions (treatable with a single 38-mm length stent), Resolute DES currently is not specifically approved or the patient subsets noted above. RESOLUTE International was not specifically designed or powered for patient subset analysis shown above.

RESOLUTE International

Performance Across Subgroups at 12 Months

<table>
<thead>
<tr>
<th>Events (%)</th>
<th>MVD</th>
<th>Diabetes</th>
<th>≤ 2.75 mm Vessels</th>
<th>&gt; 18 mm Lesions</th>
<th>Complex</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=330</td>
<td>4.0</td>
<td>3.4</td>
<td>3.5</td>
<td>3.8</td>
<td>3.7</td>
<td>4.3</td>
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<tr>
<td>N=2349</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.4</td>
<td></td>
</tr>
</tbody>
</table>

Complex patient definition: bifurcation, bypass grafts, ISR, AMI <72 hr, LVEF <30%, unprotected LM, >2 vessels stented, renal insufficiency or failure (creatinine >140 µmol/L), lesion length >27 mm, >1 lesion per vessel, lesion with thrombus or TO (preprocedure TIMI = 0). With the exception of long lesions (treatable with a single 38-mm length stent), Resolute DES currently is not specifically approved or the patient subsets noted above. RESOLUTE International was not specifically designed or powered for patient subset analysis shown above.

Belardi J. TCT 2010
RESOLUTE All Comers

Clinical Trial Design

Co-PIs: Profs. Serruys, Silber, Windecker

Open label, non-inferiority trial
Any patient with symptomatic coronary artery disease eligible for DES implantation
(no lesion/vessel limitations)

17 European sites
2300 patients randomized 1:1
Subsets: QCA 460 pts (20%); OCT 50 pts (2%)
100% monitoring

Clinical endpoints

30d 6mo 12mo 13mo 2yr 3yr 4yr 5yr

Angio/OCT endpoints

Primary Endpoint:
• 12-month target lesion failure (TLF), composite of cardiac death, target vessel MI & clinically driven TLR

Secondary Endpoints:
• Clinical: Patient composite of any death, any MI, & any repeat revascularisation
• QCA (powered): 13-month in-stent % diameter stenosis
• QCA: % diameter stenosis, late loss, and binary restenosis

Drug Therapy: ASA and clopidogrel/ticlopidine > 6mo (per guidelines)

RESOLUTE All Comers: Multi-Vessel Stenting

**TLF (Cardiac Death, Target Vessel MI, Clinically Driven TLR) at 1 Year**

<table>
<thead>
<tr>
<th></th>
<th>No. at risk</th>
<th>0</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120</th>
<th>150</th>
<th>180</th>
<th>210</th>
<th>240</th>
<th>270</th>
<th>300</th>
<th>330</th>
<th>360</th>
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<tbody>
<tr>
<td>Resolute</td>
<td>286</td>
<td>286</td>
<td>284</td>
<td>272</td>
<td>265</td>
<td>259</td>
<td>253</td>
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<td>254</td>
<td>253</td>
<td>254</td>
<td>253</td>
<td>252</td>
</tr>
<tr>
<td>Xience V</td>
<td>284</td>
<td>284</td>
<td>272</td>
<td>265</td>
<td>259</td>
<td>253</td>
<td>253</td>
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<td>253</td>
<td>249</td>
<td>249</td>
<td>246</td>
<td>246</td>
</tr>
</tbody>
</table>

Error bars indicate a point-wise two-sided 95% confidence interval (± 1.96*SE). Standard Error based on the Greenwood Formula.

RESOLUTE All Comers was not specifically designed or powered for multi-vessel subset analysis. Resolute DES is not specifically approved for the treatment of multi-vessel disease.

Log-Rank $P = 0.55$

Cumulative incidence of events [%]

Time after initial procedure [days]

Silber S. TCT 2010
RESOLUTE All Comers: STEMI Subgroup

**TLF (Cardiac Death, Target Vessel MI, Clinically Driven TLR) at 1 Year**

- **Log-Rank** $P = 0.17$

Cumulative Incidence of Events (%)

- Resolute stent (n = 119)
- Xience V stent (n = 154)

Error bars indicate a point-wise two-sided 95% confidence interval (±1.96*SE). Standard Error based on the Greenwood Formula.

RESOLUTE All Comers was not specifically designed or powered for STEMI subset analysis. Resolute DES is not specifically approved for STEMI patients.

Windecker S. TCT 2010
Results from clinical trials are not directly comparable. Information is provided for educational purposes only.
RESOLUTE

Clinical Trial Design

Pl: I. Meredith

Single De Novo Native Coronary Artery Lesions
Lesion Length: 14–27 mm
Stent Diameters: 2.5, 3.0, 3.5 mm
Stent Lengths: 18, 24, 30 mm (8/9 mm bailout)
Drug Dose: 1.6 µg/mm² stent surface area
Pre-dilatation required

Resolute Stent
n = 139

130 patients (9 additional PK Sub-Study patients enrolled after original 130 patients)
12 sites in New Zealand / Australia

Clinical endpoints

30d | 4mo | 6mo | 9mo | 12mo | 2yr | 3yr | 4yr | 5yr

Angio/IVUS endpoints

n = 30 | n = 30

Primary Endpoint: Late lumen loss (in-stent) at 9mo by QCA
Secondary Endpoints: MACE at 30d, 6, 9 and 12mo and IVUS and angiographic parameters at 9mo
30 pt subset: 4mo MACE and angiographic, IVUS parameters
Drug Therapy: ASA and clopidogrel/ticlopidine ≥ 6mo (per guidelines)
RESOLUTE Trial

Events Between Year 1 – 4

- **Events**
  - 0 events
  - 1 event
  - 2 events
  - 1 event
  - 1 event

- **TLR**
  - 0 events

- **TVR**
  - 0 events

- **Cardiac Death**
  - 0 events

- **Q-wave MI**
  - 0 events

- **ST (def/prob)**
  - 0 events

- **At 12M**
  - 1 event

- **At 24M**
  - 1 event

- **At 36M**
  - 0 events

- **At 48M**
  - 2 events
Resolute Integrity
Zotarolimus-Eluting Coronary Stent System

RESOLUTE US 12-Month Summary
RESOLUTE All Comers 2-Year Summary

ACC 2011
Resolute DES Shows Powerful Clinical Performance Across the Patient Spectrum

RESOLUTE US 12-Month Summary
- Robust trial design that enrolled a broad range of patients and lesions
  - High percentage of challenging cases: 34% diabetics and 70% small vessels
  - Resolute DES shows a very low rate of events for all safety and efficacy outcomes

RESOLUTE All Comers 2-Year Summary
- Resolute DES matches Xience V DES in all clinical endpoints at 2 years
  - No significant difference in clinical outcomes or stent thrombosis rates
- Resolute DES shows powerful performance in complex patients

Make the Complex Simple
- Revolutionary stent engineering with Resolute Integrity DES provides superior deliverability\(^1\) and better conformability\(^2\) vs. major competitors with enhanced procedural confidence

\(^{1}\)Bench test data vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES on file at Medtronic, Inc.
\(^{2}\)Simulated FEA studies Resolute Integrity DES vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES were performed by Dr. Peter Mortier, FEops / Ghent University-Belgium (Manuscript in preparation).

These tests may not be indicative of clinical performance.
RESOLUTE US Trial Design
PI: M. Leon, L. Mauri, A. Yeung

De Novo Native Coronary Lesions
Vessel Diameter: 2.25–4.00-mm
Lesion Length: ≤ 27-mm (38-mm arm: ≤ 35 mm)

Resolute DES
2.25–3.5 Clinical (n = 1242)
2.25–3.5 Angio/IVUS (n = 100)
4.0 Angio (n = 60)
38-mm Clinical (n =110–175) \(^1\)

N = 1402 patients
116 US sites

100% data monitoring
Independent data adjudication

Clinical endpoints

Angio/IVUS endpoints

Primary endpoints:
- 2.25–3.50-mm clinical → Target lesion failure at 12 months
- 2.25–3.50-mm angio/IVUS → In-stent LL at 8 months
- 4.0-mm angio → In-segment LL at 8 months
- 38-mm clinical → Target lesion failure at 12 months

Drug therapy: ASA and clopidogrel/ticlopidine ≥ 6 months (per guidelines)

RESOLUTE US 38-mm substudy is still enrolling.
Baseline Characteristics
Broad range of patients with high percentage of challenging lesions

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Resolute DES (n = 1402)</th>
<th>Lesion Characteristics</th>
<th>Resolute DES (nL = 1573)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>64</td>
<td>RVD (mm)</td>
<td>2.59 ±0.47</td>
</tr>
<tr>
<td>Men (%)</td>
<td>68</td>
<td>Minimal lumen diameter (mm)</td>
<td>0.77 ±0.35</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>34.4</td>
<td>Lesion length (mm)</td>
<td>13.06 ±5.88</td>
</tr>
<tr>
<td>Insulin dependent (%)</td>
<td>9.6</td>
<td>Lesions treated per patient</td>
<td>1.13 ±0.35</td>
</tr>
<tr>
<td>Prior MI (%)</td>
<td>21.6</td>
<td>Average DS (%)</td>
<td>70.67 ±11.52</td>
</tr>
<tr>
<td>Prior PCI (%)</td>
<td>32.7</td>
<td>Type B2/C lesion</td>
<td>75.2</td>
</tr>
<tr>
<td>Prior CABG (%)</td>
<td>8.8</td>
<td>Two vessel treated (%)</td>
<td>10.4</td>
</tr>
<tr>
<td>Mean ejection fraction (%)</td>
<td>58.0 ±9.2</td>
<td>≥1 small vessel (RVD ≤2.75 mm) (%)</td>
<td>68.5</td>
</tr>
<tr>
<td>Hyperlipidemia (%)</td>
<td>87.7</td>
<td>≥1 lesion length &gt; 18 mm (%)</td>
<td>19.9</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>84.2</td>
<td>Vessel location</td>
<td>LAD (%) 45.9</td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>20.9</td>
<td></td>
<td>LCX (%) 32.2</td>
</tr>
<tr>
<td>Stable angina (%)</td>
<td>56.1</td>
<td></td>
<td>RCA (%) 31.2</td>
</tr>
<tr>
<td>Unstable angina (%)</td>
<td>41.9</td>
<td></td>
<td>LMCA (%) 0.6</td>
</tr>
<tr>
<td>MI (%)</td>
<td>2.1</td>
<td></td>
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</tbody>
</table>
Patient Follow-Up
Robust clinical and angiographic statistical analysis of multiple study arms

Overall Population
2.25 mm – 4.0 mm stents
1402 Patients Enrolled

Clinical Cohort
N = 1242

Main Analysis Cohort
2.5 mm – 3.5 mm stent,
single lesion only
N = 1001

Main Analysis Cohort
982 (98.1%) patients
evaluable at 12 month

Angiographic Cohort
N = 160

Angiographic Cohort
150 (93.8%) patients
evaluable for angiography at 8 months

Overall Population
1376 (98.1%) patients
evaluable at 12 month
Low Rates in All Safety and Efficacy Endpoints

RESOLUTE US 12-Month Data Overall Cohort (2.25–4.00-mm diameter)

- TLF: 4.7%
- MACE: 5.5%
- ID-TLR: 2.8%
- Death: 1.3%
- Cardiac Death/TVMI: 2.0%
- ST (ARC Def/Prob): 0.1%

Resolute DES (n = 1376)
## US Trials for Second-Generation DES

<table>
<thead>
<tr>
<th></th>
<th>RESOLUTE US</th>
<th>SPIRIT III/SPIRIT IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study type</strong></td>
<td>Resolute DES pivotal study</td>
<td>SPIRIT III–Xience V pivotal study</td>
</tr>
<tr>
<td></td>
<td>Nonrandomised multistudy trial</td>
<td>SPIRIT IV–more complex population</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Both randomised to Taxus Express</td>
</tr>
<tr>
<td><strong>N, sites</strong></td>
<td>1402 Resolute DES patients</td>
<td>SPIRIT III–669 Xience V pt; 65 US sites</td>
</tr>
<tr>
<td></td>
<td>116 US sites</td>
<td>SPIRIT IV–2458 Xience V pt; 66 US sites</td>
</tr>
<tr>
<td><strong>Multivessel treatment</strong></td>
<td>Up to 2 vessel treatments</td>
<td>SPIRIT III–up to 2 vessels</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SPIRIT IV–up to 3 vessels</td>
</tr>
<tr>
<td><strong>Angiographic follow-up</strong></td>
<td>8 mo for angio cohort (n = 160)</td>
<td>SPIRIT III–8 mo all patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SPIRIT IV–none</td>
</tr>
<tr>
<td><strong>Lesion/stent sizes (mm)</strong></td>
<td>2.25–4.00 (diameter) Up to 38 (length)</td>
<td>2.50–3.75 (diameter) Up to 28 (length)</td>
</tr>
<tr>
<td><strong>Primary endpoint</strong></td>
<td>TLF at 12 mo</td>
<td>SPIRIT III–LL at 8 mo; SPIRIT IV–TLF at 12 mo</td>
</tr>
<tr>
<td><strong>Diabetes mellitus (%)</strong></td>
<td>34.4 (9.6 IDDM)</td>
<td>SPIRIT III–29.6; (7.8 IDDM)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SPIRIT IV–32.0; (8.5 IDDM)</td>
</tr>
<tr>
<td><strong>Prior MI (%)</strong></td>
<td>21.6</td>
<td>SPIRIT III–19.9; SPIRIT IV–21</td>
</tr>
<tr>
<td><strong>Unstable angina (%)</strong></td>
<td>41.9</td>
<td>SPIRIT III–18.7; SPIRIT IV–27.7</td>
</tr>
<tr>
<td><strong>RVD (mm)</strong></td>
<td>2.59</td>
<td>SPIRIT III–2.77; SPIRIT IV–2.75</td>
</tr>
<tr>
<td><strong>Lesion length (mm)</strong></td>
<td>13.06 ± 5.88</td>
<td>SPIRIT III–14.7; SPIRIT IV–14.8 ± 6.7</td>
</tr>
<tr>
<td><strong>Age (yr)/men (%)</strong></td>
<td>64/68</td>
<td>SPIRIT III–63.2/70.1; SPIRIT IV–63.3/67.7</td>
</tr>
</tbody>
</table>
Clinical Outcomes: RESOLUTE US Overall Cohort

All patients from RESOLUTE US (2.25–4.00-mm diameter)
All patients from SPIRIT III and SPIRIT IV (2.50–3.75-mm diameter)

12-Month Results

<table>
<thead>
<tr>
<th></th>
<th>RESOLUTE US (n = 1376)</th>
<th>SPIRIT III, Xience V DES (n = 595)</th>
<th>SPIRIT IV, Xience V DES (n = 2328)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>1.5</td>
<td>1.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>0.7</td>
<td>0.8</td>
<td>0.4</td>
</tr>
<tr>
<td>ST (ARC Def/Prob)</td>
<td>0.1</td>
<td>1.1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Results come from separate clinical trials. Data may differ in a head-to-head comparison.
Clinical Outcomes: RESOLUTE US Main Cohort

Main cohort from RESOLUTE US (2.50–3.50-mm diameter)
All patients from SPIRIT III and SPIRIT IV (2.50–3.75-mm diameter)

<table>
<thead>
<tr>
<th>12-Month Results</th>
<th>RESOLUTE US (n = 1093)</th>
<th>SPIRIT III, Xience V DES (n = 595)</th>
<th>SPIRIT IV, Xience V DES (n = 2328)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>1.6 (1.9)</td>
<td>0.8 (0.4)</td>
<td>0.3 (0.4)</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>2.8 (1.9)</td>
<td>0.8 (0.4)</td>
<td>0.3 (0.4)</td>
</tr>
<tr>
<td>ST (ARC Def/Prob)</td>
<td>2.5 (2.2)</td>
<td>1.1 (1.1)</td>
<td>0.3 (0.3)</td>
</tr>
<tr>
<td>ID-TLR</td>
<td>3.3 (3.3)</td>
<td>1.6 (1.6)</td>
<td>0.3 (0.3)</td>
</tr>
</tbody>
</table>

Results come from separate clinical trials. Data may differ in a head-to-head comparison.
Innovative Trial Design
Large, real-world study that reflects complexities of daily clinical practice

RESOLUTE All Comers Trial Design

Open-label, noninferiority trial
All patients with symptomatic coronary artery disease eligible for DES implantation
(no lesion/vessel limitations)

Co-PIs: Profs. Serruys, Silber, Windecker
2300 patients, 17 sites in Europe
100% monitoring

Resolute DES
n = 1150

Xience V DES
n = 1150

Clinical
30 d 6 mo 12 mo 13 mo 2 yr 3 yr 4 yr 5 yr

Angio/OCT

Primary endpoint: TLF (ARC-defined): cardiac death, target vessel MI, TLR at 12 mo
Secondary endpoint (powered): % diameter stenosis (in-stent) at 13 mo
Secondary endpoints: TLF at 30 days, 6 mo, 2–5 yr; composite (all death, all MI, any revascularisation)
at each FU time point; angiographic and optical coherence tomography (OCT) parameters at 13 mo
Drug therapy: ASA and clopidogrel/ticlid >6 mo (per guidelines)
Excellent Clinical Follow-Up at 2 Years

Patients Enrolled
N = 2292 (N_L = 3366)

Resolute (ZES)
n = 1140

Clinical F/U (1 yr)
1130/1140
99.1%

Clinical F/U (2 yr)
1121/1140
98.3%

Randomized

Xience-V (EES)
n = 1152

Clinical F/U (1 yr)
1138/1152
98.8%

Clinical F/U (2 yr)
1128/1152
97.9%
Resolute DES Continues to Match Xience V DES in Primary Endpoint at 2 Years

TARGET LESION FAILURE

Resolute DES (N=1140)  Xience V DES (N=1152)

Log Rank $p = 0.73$

$\text{TLF} = \text{cardiac death, target vessel MI, TLR}$

Error bars indicate a pointwise, two-sided 95% confidence interval (1.96 ± SD).
Standard error is based on the Greenwood formula.
Similar Results in All Efficacy and Safety Endpoints at 2 Years

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Resolute DES</th>
<th>Xience V DES</th>
</tr>
</thead>
<tbody>
<tr>
<td>ID-TLR (%)</td>
<td>5.7</td>
<td>5.1</td>
</tr>
<tr>
<td>TVR (%)</td>
<td>7.3</td>
<td>6.9</td>
</tr>
<tr>
<td>Death (%)</td>
<td>3.2</td>
<td>4.0</td>
</tr>
<tr>
<td>CD (%)</td>
<td>2.6</td>
<td>2.2</td>
</tr>
<tr>
<td>TV MI (%)</td>
<td>4.7</td>
<td>4.5</td>
</tr>
</tbody>
</table>

- Values are based on Fisher Exact Test.
- Values for outcome differences are unadjusted for multiple comparisons.
- RESOLUTE All Comers was not specifically designed or powered to individually compare endpoints shown above.
No Significant Difference in Stent Thrombosis Rates

ARC Definite/Probable ST Rate

Resolute DES (N = 1140) vs. Xience V DES (N = 1152)

Log Rank $p = 0.08$

Resolute DES overall ST rate driven primarily by events in the first 5 days

RESOLUTE All Comers was not specifically designed or powered to individually compare endpoints shown above.
No Difference in Very Late Stent Thrombosis (VLST)

No difference in VLST rates

\[ p = 1.0 \]

No difference in DAPT compliance

<table>
<thead>
<tr>
<th>Length of DAPT</th>
<th>Resolute ZES</th>
<th>Xience V EES</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 days on (%)</td>
<td>93.8</td>
<td>94.6</td>
<td>0.419</td>
</tr>
<tr>
<td>180 days on (%)</td>
<td>93.1</td>
<td>93.3</td>
<td>0.933</td>
</tr>
<tr>
<td>360 days on (%)</td>
<td>84.1</td>
<td>83.8</td>
<td>0.908</td>
</tr>
<tr>
<td>720 days on (%)</td>
<td>18.6²</td>
<td>18.1²</td>
<td>0.781</td>
</tr>
</tbody>
</table>

\( p \)-Values are based on Fisher Exact Test.
\( p \)-Values for outcome differences are unadjusted for multiple comparisons.
RESOLUTE All Comers was not specifically designed or powered to individually compare endpoints shown above.
\( ^2 \)Majority on DAPT considered complex or ACS at time of procedure
Stent Thrombosis Rates for Resolute DES Across the Patient Spectrum

ARC Definite/Probable ST 12-Month Data

- Resolute DES

All Comers Trials

RESOLUTE All Comers N = 1140
RESOLUTE International N = 2349
ISAR TEST 5 N = 1000
RISICO N = 820

Approval Trials

RESOLUTE US N = 1402
RESOLUTE FIM N = 130

Studies not powered for this low-frequency ST event.
Almost 70% of RESOLUTE All Comers Patients are Complex

### All Patients

<table>
<thead>
<tr>
<th></th>
<th>Resolute DES N = 1140 (%)</th>
<th>Xience V DES N = 1152 (%)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complex</td>
<td>67.0</td>
<td>65.6</td>
<td>NS</td>
</tr>
<tr>
<td>AMI (within 72 hours)</td>
<td>28.9</td>
<td>28.8</td>
<td>NS</td>
</tr>
<tr>
<td>Multivessel treatment (&gt;2)</td>
<td>25.1</td>
<td>24.7</td>
<td>NS</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>4.0</td>
<td>3.1</td>
<td>NS</td>
</tr>
<tr>
<td>ISR</td>
<td>8.1</td>
<td>8.0</td>
<td>NS</td>
</tr>
<tr>
<td>Bifurcation</td>
<td>16.9</td>
<td>17.7</td>
<td>NS</td>
</tr>
<tr>
<td>Unprotected left main</td>
<td>1.6</td>
<td>1.3</td>
<td>NS</td>
</tr>
<tr>
<td>Bypass graft</td>
<td>2.5</td>
<td>2.4</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF &lt;30%</td>
<td>2.8</td>
<td>2.1</td>
<td>NS</td>
</tr>
<tr>
<td>Long lesion (&gt;27 mm)</td>
<td>5.7</td>
<td>6.0</td>
<td>NS</td>
</tr>
<tr>
<td>Total occlusion</td>
<td>16.3</td>
<td>17.2</td>
<td>NS</td>
</tr>
<tr>
<td>&gt;1 lesion per vessel</td>
<td>16.4</td>
<td>17.7</td>
<td>NS</td>
</tr>
<tr>
<td>Thrombus lesion</td>
<td>7.4</td>
<td>6.9</td>
<td>NS</td>
</tr>
</tbody>
</table>

With the exception of long lesions (treatable with a single 38-mm length stent), Resolute DES currently is not specifically approved for the patient subsets noted in this complex patient definition.
Resolute Strength: Powerful Performance in Complex Patients at 2 Years

Complex patient definition: Bifurcation, SVG, ISR, AMI <72 hr, LVEF <30%, unprotected LM, >2 vessels stented, renal insufficiency or failure (creatinine >140 µmol/L), lesion length >27 mm, >1 lesion/vessel, lesion with thrombus or TO (preprocedure TIMI = 0). Currently, Resolute DES is not specifically approved for the subsets noted in this complex patient definition.

p-Values are based on Fisher Exact Test. p-Values for outcome differences are unadjusted for multiple comparisons. RESOLUTE All Comers was not specifically designed or powered for complex patient subset analysis.
Resolute Integrity DES Provides Identical Drug Delivery to Resolute DES

This is achieved by having highly similar:

- Surface area
- Scaffolding
- Strut thickness
- Cell area
- Drug load and drug distribution
- Drug elution

*In-vivo* elution\(^3\) results for Resolute Integrity DES provide confidence that you can expect the same powerful clinical performance as Resolute DES.

\(^{3}\)Porcine coronary artery model. Data on file at Medtronic, Inc. and may not be indicative of clinical performance.
The Resolute Integrity stent’s unique helical design and new delivery system provide **breakthrough deliverability that is superior to leading DES.**
Comparison of Device Performance for Market-Leading DES

<table>
<thead>
<tr>
<th></th>
<th>Resolute Integrity DES</th>
<th>Xience Prime DES</th>
<th>Promus Element DES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LESION ACCESS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trackability</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Crossing profile</td>
<td>✓</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td>Pushability</td>
<td>✓</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td><strong>PLACEMENT ACCURACY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiopacity</td>
<td>✓</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td>Stent foreshortening</td>
<td>✓</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td><strong>LESION COVERAGE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scaffolding</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>Radial strength</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>Strut apposition</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td><strong>ANATOMICALLY COMPLEX LESIONS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sidebranch access</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>Vessel conformability&lt;sup&gt;4&lt;/sup&gt;</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
</tr>
</tbody>
</table>

Resolute Integrity DES redefines performance.

Bench test data on file at Medtronic
<sup>4</sup>Simulated FEA studies Resolute Integrity DES vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES were performed by Dr. Peter Mortier, FEops/Ghent University, Belgium (manuscript in preparation). These tests may not be indicative of clinical performance.
Summary & Conclusion

Resolute DES Shows Powerful Clinical Performance Across the Patient Spectrum

RESOLUTE US 12-Month Summary
- Robust trial design that enrolled a broad range of patients and lesions
  - High percentage of challenging cases: 34% diabetics and 70% small vessels
  - Resolute DES shows a very low rate of events for all safety and efficacy outcomes

RESOLUTE All Comers 2-Year Summary
- Resolute DES matches Xience V DES in all clinical endpoints at 2 years
  - No significant difference in clinical outcomes or stent thrombosis rates
- Resolute DES shows powerful performance in complex patients

Make the Complex Simple
- Revolutionary stent engineering with Resolute Integrity DES provides superior deliverability\(^1\) and better conformability\(^2\) vs. major competitors with enhanced procedural confidence

Powerful clinical performance with superior deliverability

RESOLUTE US and All Comers trials studied Resolute DES.
RESOLUTE All Comers was not specifically designed or powered for complex patient subset analysis.
\(^1\)Bench test data vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES on file at Medtronic, Inc.
\(^2\)Simulated FEA studies Resolute Integrity DES vs. Abbott Xience Prime DES and Boston Scientific Promus Element DES were performed by Dr. Peter Mortier, FEops / Ghent University-Belgium (Manuscript in preparation). These tests may not be indicative of clinical performance.