The XIENCE Short DAPT Program:

XIENCE 90/28

Evaluating the Safety of 3-month and 1-month DAPT in HBR Patients

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on Behalf of the XIENCE 90/28 Investigators
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Professor of Cardiology, University of Bern, Bern, Switzerland
@vlgmrc
Disclosure Statement of Financial Interest

Within the past 12 months, I, **Roxana Mehran**, or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultant / Advisory / Speaking Engagements</td>
<td>Abbott Laboratories (to institution), Abiomed (spouse), Boston Scientific, Idorsia Pharmaceuticals Ltd. (no fee), Janssen, Medscape/WebMD, Medtelligence (Janssen Scientific Affairs), Roivant Sciences Inc, Sanofi, Siemens Medical Solutions, Regeneron Pharmaceuticals (no fee), Spectranetics/Philips/Volcano Corp (to institution), The Medicines Company (spouse)</td>
</tr>
<tr>
<td>Research Funding to Institution</td>
<td>Abbott Laboratories, Abiomed, AstraZeneca, Bayer, Beth Israel Deaconess, BMS, CERC, Chiesi, Concept Medical, CSL Behring, DSI, Medtronic, Novartis, OrbusNeich</td>
</tr>
<tr>
<td>Scientific Advisory Board</td>
<td>Bristol-Myers Squibb (to institute), Medtelligence (Janssen Scientific Affairs), Merck (spouse)</td>
</tr>
<tr>
<td>Equity, &lt;1%</td>
<td>Claret Medical, Elixir Medical</td>
</tr>
<tr>
<td>DSMB Membership Paid to Institution</td>
<td>Watermark Research Partners</td>
</tr>
<tr>
<td>Associate Editor</td>
<td>ACC, AMA</td>
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</table>
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<tr>
<td>Grant/Research Support</td>
<td>Daiichi Sankyo, Medicure, Terumo, CoreFLOW</td>
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<tr>
<td>Consulting Fees/Honoraria</td>
<td>Abbott, Alvimedica/CID, Astra Zeneca, Bayer, CoreFLOW, Chiesi, IDORSIA, Bristol Myers Squib SA, Medscape, Vesalio, Universität Basel Dept. Klinische Forschung</td>
</tr>
<tr>
<td>Major Stock Shareholder/Equity</td>
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<td>Royalty Income</td>
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<td>Ownership/Founder</td>
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<td>Intellectual Property Rights</td>
<td>None</td>
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<tr>
<td>Other Financial Benefit</td>
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Background

• DAPT is essential for the prevention of ischemic events after PCI but inevitably increases the risk of bleeding

• Patients at high bleeding risk (HBR) constitute up to 40% of subjects undergoing PCI

• As hemorrhagic events following PCI have substantial prognostic implications, bleeding-avoidance strategies are vital to improve patient outcomes

• Recent trials on next-generation DES have shown an acceptable safety profile with a short course of DAPT; however, the optimal DAPT duration in HBR patients remains unknown

Stent Platform

Multilink Stent Design
CoCr L-605 Alloy
Strut thickness: 81 μm

Polymer Coating

Durable Fluoropolymer Coating
Fluoropassivation properties selectively retain albumin and minimize platelet adhesion

Drug

Everolimus
Average drug concentration: 100 μg/cm²
Study Hypotheses

In HBR patients who have undergone successful PCI with the XIENCE stent and completed a short DAPT regimen of 1 month (XIENCE 28) or 3 months (XIENCE 90) without experiencing adverse ischemic events, continued treatment with aspirin monotherapy would be non-inferior to DAPT for up to 12 months with respect to ischemic events and superior with respect to bleeding.
Trial Objectives

Among HBR patients who have undergone successful PCI with the XIENCE stent:

Primary Objective:
- To evaluate the safety (all death or MI) of a short DAPT regimen (1 or 3 months) versus DAPT for up to 12 months

Secondary Objectives:
- To determine the impact of short DAPT (1 or 3 months) versus DAPT for up to 12 months on clinically relevant bleeding (BARC 2-5)
- To evaluate stent thrombosis (definite/probable) against a performance goal*

* Only for XIENCE 90
XIENCE Short DAPT Program

3-month DAPT
101 sites in USA
2,047 patients

1-month DAPT
52 sites
963 patients

Global

USA
58 sites
642 patients

TOTAL OF ~3,600 PATIENTS WITH 1-MONTH OR 3-MONTH DAPT
# Short DAPT Program Organization

<table>
<thead>
<tr>
<th>Role</th>
<th>Members</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PIs</strong></td>
<td>Dr. Roxana Mehran&lt;br&gt;Dr. Marco Valgimigli</td>
</tr>
<tr>
<td><strong>Executive Committee</strong></td>
<td>Drs. Dominick J. Angiolillo, Sripal Bangalore, Deepak L. Bhatt, Junbo Ge, James Hermiller, Rajendra R. Makkar, Franz-Josef Neumann, Shigeru Saito, Marco Valgimigli, Roxana Mehran</td>
</tr>
<tr>
<td><strong>Steering Committee</strong></td>
<td>Drs. Jose M De La Torre Hernandez, Vijay Kunadian, Gennaro Sardella, Holger Thiele, Olivier Varenne, Pascal Vranckx, Stephan Windecker, Yujie Zhou</td>
</tr>
<tr>
<td><strong>Independent Biostatistician</strong></td>
<td>Dr. Joseph Massaro (Boston University)</td>
</tr>
<tr>
<td><strong>DSMB</strong></td>
<td>Axio Research</td>
</tr>
<tr>
<td><strong>CEC</strong></td>
<td>Cardiovascular Research Foundation</td>
</tr>
<tr>
<td><strong>Sponsor</strong></td>
<td>Abbott</td>
</tr>
</tbody>
</table>
Participating Sites

XIENCE 28 USA
58 Sites U.S. & Canada

XIENCE 28 Global
52 Sites Europe & Asia

XIENCE 90
101 Sites U.S.
Key Inclusion Criteria

HBR Criteria

- Age $\geq 75$ years
- Chronic OAC therapy
- CKD (creatinine $\geq 2.0$ mg/dl or dialysis)
- Anemia (hemoglobin $<11$ g/dl)
- Hematological disorders (platelet count $<100,000$/mm$^3$ or any coagulation disorder)
- Major bleeding in the last 12 months
- History of stroke

Angiographic Criteria

- Successful PCI
- Exclusive use of XIENCE stents
- Target vessel diameter of 2.25 - 4.25 mm
- Target lesion $\leq 32$ mm in length*
- $\leq 3$ target lesions with $\leq 2$ target lesions per vessel

* Only for XIENCE 90
Key Exclusion Criteria

**Clinical Criteria**
- STEMI presentation
- LVEF <30%
- Planned surgery within 1 or 3 months* of PCI

**Angiographic Criteria**
- Target lesion containing thrombus†
- PCI with overlapping stents
- Target lesion in one of the following:
  - left main coronary artery
  - arterial or saphenous vein graft
  - in-stent restenosis
  - chronic total occlusion

* 1 month in XIENCE 28; 3 months in XIENCE 90
† Only for XIENCE 90
**Trial Design**

A prospective, single-arm, multicenter, open-label, non-randomized trial

**X90**

1. **Enrollment**
   - Baseline
2. **Index PCI**
3. **P2Y12 inhibitor + ASA**
4. **Stop P2Y12 inh. if event-free†**
   - 3 M
   - Primary EP
   - Follow-up
   - 6 M
   - End of study 12 M
5. **Primary analysis period:** from 3 to 12 months

**X28**

1. **Enrollment**
   - Baseline
2. **Index PCI**
3. **P2Y12 inhibitor + ASA**
4. **Stop P2Y12 inh. if event-free†**
   - 1 M
   - Primary EP Follow-up
   - 6 M
   - End of study 12 M

**Primary EP Follow-up**

**Primary analysis period:** from 1 to 6 months

---

* For patients on chronic OAC, dual therapy (OAC plus P2Y\(_{12}\) inhibitor) might be considered for the first 1 or 3 months

† “Event-free” defined as free from MI, repeat revascularization, stroke, or ST and compliant with DAPT in the first 1 or 3 months
## Patient Disposition

### XIENCE 90

- **Total enrolled**
  - N = 2047

- **Follow-up at 3 months**
  - N = 1923/2047 (93.9%)

  - 37 Deaths
  - 44 Missed Visit
  - 43 Withdrawn by patient or site/physician

  - **“3-month clear” assessment**

  - **“3-month clear” patients**
    - N = 1693/1923 (88.0%)

  - 230 (12.0%) not 3-month clear:
    - 54 AE before 3 mo
    - 109 DAPT non-compliance
    - 73 Continued P2Y₁₂ after 3 mo
    - 1 Withdrawn by patient

  - **Follow-up at 12 months**
    - N = 1653/1693 (97.6%)

  - 18 LTFU/Missed Visit
  - 22 Withdrawn by patient or site/physician

### XIENCE 28

- **Total enrolled**
  - N = 1605

- **Follow-up at 1 months**
  - N = 1546/1605 (96.3%)

  - 11 Deaths
  - 12 LTFU/Missed visit
  - 1 Duplicate subject enrollment
  - 35 Withdrawn by patient or site/physician

  - **“1-month clear” assessment**

  - **“1-month clear” patients**
    - N = 1392/1546 (90.0%)

  - 154 (10%) not 1-month clear:
    - 25 With AE before 1 mo
    - 35 DAPT Non-Compliance
    - 134 Physician’s Concern
    - 6 Continued P2Y₁₂ after 1 mo

  - **Follow-up at 6 months**
    - N = 1375/1392 (98.8%)

  - 10 Missed Visit
  - 6 Withdrawn by patient
  - 1 Other

---

* “Clear” defines patients who are event free (MI, repeat revascularization, stroke, or ST) and compliant with DAPT within 1 month (XIENCE 28) or 3 months (XIENCE 90) of index PCI
HBR Criteria Distribution

All Registered Patients

XIENCE 90

- Age ≥ 75 years: 65.6%
- Age ≥ 75 years (only): 35.5%
- Chronic OAC therapy: 40.8%
- Hemoglobin <11 g/dL: 16.2%
- History of stroke: 11.3%
- Creatinine ≥2.0 mg/dL: 8.0%
- Platelet <100,000/mm3: 3.0%
- History of major bleeding: 2.9%

XIENCE 28

- Age ≥ 75 years: 69.3%
- Age ≥ 75 years (only): 35.1%
- Chronic OAC therapy: 43.9%
- Hemoglobin <11 g/dL: 15.2%
- History of stroke: 10.8%
- Creatinine ≥2.0 mg/dL: 8.6%
- Platelet <100,000/mm3: 3.9%
- History of major bleeding: 3.6%

AVERAGE NUMBER OF CRITERIA MET: 1.5 ± 0.7

AVERAGE NUMBER OF CRITERIA MET: 1.6 ± 0.8
# Baseline Characteristics

## “Clear” Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>XIENCE 90 (N = 1693)</th>
<th>XIENCE 28 (N = 1392)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (Mean ± SD)</td>
<td>75.25 ± 9.29 (1693)</td>
<td>75.97 ± 8.37 (1392)</td>
</tr>
<tr>
<td>Female</td>
<td>35.2% (596/1693)</td>
<td>32.5% (453/1392)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>89.5% (1516/1693)</td>
<td>84.7% (1179/1392)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>82.8% (1401/1693)</td>
<td>67.5% (939/1392)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>39.2% (663/1692)</td>
<td>37.0% (512/1382)</td>
</tr>
<tr>
<td>CKD (eGFR &lt; 60 mL/min)</td>
<td>40.2% (677/1682)</td>
<td>47.4% (631/1330)</td>
</tr>
<tr>
<td>Prior MI</td>
<td>15.8% (264/1669)</td>
<td>16.4% (227/1382)</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>12.1% (205/1693)</td>
<td>8.0% (112/1392)</td>
</tr>
<tr>
<td>ACS</td>
<td>34.7% (588/1693)</td>
<td>34.1% (475/1392)</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>7.1% (120/1693)</td>
<td>17.6% (245/1392)</td>
</tr>
<tr>
<td>Unstable Angina</td>
<td>28.7% (486/1693)</td>
<td>16.5% (230/1392)</td>
</tr>
<tr>
<td>PARIS Score (Median, IQR)</td>
<td>6.0 (4.0, 8.0) (1693)</td>
<td>6.0 (4.0, 8.0) (1392)</td>
</tr>
<tr>
<td>PRECISE-DAPT Score (Median, IQR)</td>
<td>25.0 (19.0, 32.0) (1606)</td>
<td>27.0 (20.0, 34.0) (1295)</td>
</tr>
</tbody>
</table>
### Procedural Characteristics

#### “Clear” Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>XIENCE 90 (N = 1693)</th>
<th>XIENCE 28 (N = 1392)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivessel Disease</td>
<td>46.0% (779/1693)</td>
<td>41.2% (573/1392)</td>
</tr>
<tr>
<td>Radial Access</td>
<td>52.2% (883/1693)</td>
<td>70.8% (986/1392)</td>
</tr>
<tr>
<td>B2/C Lesion</td>
<td>33.8% (573/1693)</td>
<td>35.8% (498/1392)</td>
</tr>
<tr>
<td>Bifurcation</td>
<td>7.6% (129/1693)</td>
<td>11.6% (161/1392)</td>
</tr>
<tr>
<td>Total Stent Length, mm (Mean ± SD)</td>
<td>25.5 ± 13.8 (1693)</td>
<td>27.2 ± 14.4 (1389)</td>
</tr>
</tbody>
</table>

N = 2078 Lesions

<table>
<thead>
<tr>
<th>Target Lesion Location</th>
<th>XIENCE 90 (N = 1693)</th>
<th>XIENCE 28 (N = 1392)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>43.2% (898/2078)</td>
<td>45.9% (781/1700)</td>
</tr>
<tr>
<td>LCX</td>
<td>24.7% (513/2078)</td>
<td>24.1% (409/1700)</td>
</tr>
<tr>
<td>RCA</td>
<td>32.0% (665/2078)</td>
<td>29.9% (509/1700)</td>
</tr>
<tr>
<td>Pre-procedure RVD, mm (Mean ± SD)</td>
<td>2.99 ± 0.49 (2078)</td>
<td>2.99 ± 0.50 (1700)</td>
</tr>
<tr>
<td>Pre-procedure DS, % (Mean ± SD)</td>
<td>83.7 ± 10.3 (2078)</td>
<td>82.47 ± 10.80 (1699)</td>
</tr>
<tr>
<td>Target Lesion Length, mm (Mean ± SD)</td>
<td>16.0 ± 7.1 (2078)</td>
<td>18.01 ± 8.43 (1700)</td>
</tr>
</tbody>
</table>
Antiplatelet Usage

Primary Analysis Population

XIENCE 90
Between 3 and 12 Months

Notes:
- ASA: includes subjects on ASA only or ASA + OAC
- DAPT: includes subjects on DAPT only or DAPT + OAC
- P2Y₁₂ inh.: includes subjects on P2Y₁₂ inh. and/or OAC

Note: Patients with adverse events during follow-up are included in the curves
Study Endpoints

Primary endpoint
• All-cause death or all MI (non-inferiority)  
  

Key secondary endpoints
• BARC 2-5 bleeding (superiority)  
• Definite/probable ST (performance goal) – XIENCE 90 only
XIENCE V USA: Historical Control

A prospective, multicenter, post-approval study to evaluate the safety and effectiveness of the XIENCE stent in real-world settings between 2008-2011

8,061 patients from 192 sites in the US

**DAPT Usage in XV USA**

<table>
<thead>
<tr>
<th>Visit</th>
<th>Usage</th>
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</thead>
<tbody>
<tr>
<td>30-day</td>
<td>94.2%</td>
</tr>
<tr>
<td>180-day</td>
<td>90.5%</td>
</tr>
<tr>
<td>1-Year</td>
<td>85.6%</td>
</tr>
</tbody>
</table>

**A Real-World Population**

- Age: $64.6 \pm 10.8$ y
- Diabetes: 35.8%
- Renal Insufficiency: 10.5%
- Prior MI: 29.7%
- Male: 69.6%
- LVEF <30%: 3.4%
- AMI on Presentation: 14.8%
- Bifurcation Lesion: 9.7%
- Restenosis: 8.8%
- Prior CABG: 16.4%
- B2/C Lesion: 49.9%
- Multivessel Disease: 39.8%
- Prior PCI: 39.1%
- Graft Lesion: 4.6%

Naidu S.N. et al., J Am Coll Cardiol Intv 2012;5:626 –35
Propensity Score Stratification: XIENCE 90

**POPULATIONS**

- XIENCE 90 (3-mo DAPT)
  - Investigational Arm
- XIENCE V USA (12-mo DAPT)
  - Historical Control

**PROPENSITY STRATIFICATION**

Patients sorted by propensity score using baseline characteristics

**GROUPING BY PROPENSITY SCORE**

<table>
<thead>
<tr>
<th>Stratification in 5 quintiles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
</tr>
<tr>
<td>Q2</td>
</tr>
<tr>
<td>Q3</td>
</tr>
<tr>
<td>Q4</td>
</tr>
<tr>
<td>Q5</td>
</tr>
</tbody>
</table>

XIENCE 90 XV USA
Propensity Score Stratification: XIENCE 28

**POPULATIONS**

- **XIENCE 28 (1-mo DAPT)**
  - Investigational Arm

- **XIENCE V USA (6-mo DAPT)**
  - Historical Control

**PROPENSITY STRATIFICATION**

Patients sorted by propensity score using baseline characteristics

**GROUPING BY PROPENSITY SCORE**

- **XIENCE 28**
  - Q1
  - Q2
  - Q3
  - Q4
  - Q5

- **XV USA**
  - Q1
  - Q2
  - Q3
  - Q4
  - Q5
## Sample Size and Power Calculations

**Primary Endpoint: All Death or MI**

<table>
<thead>
<tr>
<th></th>
<th>XIENCE 90</th>
<th>XIENCE 28</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control group</strong></td>
<td>3-month clear HBR patients from XIENCE V USA</td>
<td>1-month clear HBR patients from XIENCE V USA</td>
</tr>
<tr>
<td><strong>Primary hypothesis</strong></td>
<td>Non-inferiority for all death or MI</td>
<td>Non-inferiority for all death or MI</td>
</tr>
<tr>
<td></td>
<td>• Margin ($\Delta$) = 2.8%</td>
<td>• Margin ($\Delta$) = 2.5%</td>
</tr>
<tr>
<td><strong>Expected rate</strong></td>
<td>6.1% between 3 and 12 months</td>
<td>4.3% between 1 and 6 months</td>
</tr>
<tr>
<td><strong>Statistical model</strong></td>
<td>Propensity stratification</td>
<td>Propensity stratification</td>
</tr>
<tr>
<td><strong>Test significance level ($\alpha$)</strong></td>
<td>0.025 (1-sided)</td>
<td>0.025 (1-sided)</td>
</tr>
<tr>
<td><strong>Attrition rate</strong></td>
<td>15%</td>
<td>10%</td>
</tr>
<tr>
<td><strong>Power (1-$\beta$)</strong></td>
<td>87%</td>
<td>90%</td>
</tr>
<tr>
<td><strong>Sample size (N patients)</strong></td>
<td>2000</td>
<td>1600</td>
</tr>
</tbody>
</table>
XIENCE 90: All Death or MI
Between 3 and 12 Months

PS Stratified Mean

Non-inferiority Analysis

<table>
<thead>
<tr>
<th>XIENCE 90 (N = 1693)</th>
<th>5.4%</th>
</tr>
</thead>
<tbody>
<tr>
<td>XIENCE V USA (N = 1280)</td>
<td>5.4%</td>
</tr>
</tbody>
</table>

Non-inferiority tested with the stratified Farrington-Manning method

One-sided 97.5%
UCL: 2.23%

$P_{\text{non-inferiority}} = 0.0063$

Non-inferiority margin: 2.8%
XIENCE 28: All Death or MI

Between 1 and 6 Months

PS Stratified Mean

Mean rate across 5 quintiles (%)

- 0%
- 2%
- 4%
- 6%
- 8%
- 10%

XIENCE 28 (N = 1392)
- 3.5%

XIENCE V USA (N = 1411)
- 4.3%

Non-inferiority Analysis

One-sided 97.5%
UCL: 0.97%

$P_{\text{non-inferiority}} = 0.0005$

Non-inferiority margin: 2.5%

Non-inferiority tested with the stratified Farrington-Manning method
An assumed ~50% reduction in BARC 2-5 bleeding provided XIENCE 90 with 95% power and XIENCE 28 with 90% power. Superiority tested with the stratified Farrington-Manning method using a one-sided significance level of 0.025.
The PS stratified analysis for BARC 3-5 bleeding was not pre-specified.
XIENCE 90: Stent Thrombosis

Powered Secondary Endpoint (3-12 Months)

ARC Definite/Probable ST

Performance Goal: 1.2%

2-sided 95% UCL: 0.63%

$P < 0.0001$

0.20% (4/1635)

An assumed 0.5% rate of definite/probable ST provided XIENCE 90 with 85% power (Exact test)
XIENCE 28: Stent Thrombosis

ARC Definite/Probable ST
Between 1 and 6 Months

Definite/probable ST was not a powered secondary endpoint in XIENCE 28

<table>
<thead>
<tr>
<th></th>
<th>XIENCE 28</th>
<th>XIENCE V USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-PS Stratified Rates (%)</td>
<td>0.3%</td>
<td>0.3%</td>
</tr>
<tr>
<td></td>
<td>4/1361</td>
<td>4/1387</td>
</tr>
</tbody>
</table>
Limitations

• The XIENCE 90 and XIENCE 28 studies present limitations inherent to the non-randomized design, despite statistical compensation using a propensity-adjusted analysis.

• Findings may not be generalizable to patients who do not meet the XIENCE Short DAPT Program inclusion and exclusion criteria.

• The observed treatment effect applies only to patients “free” from adverse events and adherent to the DAPT regimen in the first 1 or 3 months post-PCI.

• Given that XIENCE V USA was performed approximately one decade before the XIENCE Short DAPT Program, confounders related to changes in clinical practice cannot be excluded.
Conclusions

Among HBR patients undergoing PCI with the XIENCE stent, a short DAPT regimen of 1 or 3 months compared with standard DAPT up to 12 months resulted in:

• non-inferior ischemic outcomes
• similar rates of clinically relevant (BARC 2-5) bleeding, with a significant reduction in major (BARC 3-5) bleeding
• very low incidence of stent thrombosis
**XIENCE 90**

- **Royal Jubilee Hospital**  
  PI: Dr. Simon Robinson  
  RC: Noreen Lounsbury

- **Redmond Regional Medical Center**  
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  RC: Kathy Jones

- **Heart Center Research, LLC**  
  PI: Dr. Henry Chen  
  RC: Karen Hensley

- **Anmed Health**  
  PI: Dr. Brent McLaurin  
  RC: Charlesa Davis

- **Baylor Scott & White Heart and Vascular Hospital**  
  PI: Dr. James Choi  
  RC: Angela Roy

- **Cardiovascular Research Institute of Kansas**  
  PI: Dr. Aziz Maksoud  
  RC: Lindsey Steele

**XIENCE 28 USA**

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  RC: Friederike Geyer

- **Az.Osp. Universitaria di Ferrara**  
  PI: Dr. Gianluca Campo  
  RC: Veronica Lodolini

- **Elisabeth-Krankenhaus Essen GmbH**  
  PI: Dr. Thomas Schmitz  
  RC: Melanie Steffen

- **Centro Cardiologico Monzino**  
  PI: Dr. Daniela Trabattoni

- **Herzzentrum Leipzig GmbH**  
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  RC: Eva Kirchhof

- **Universitatsmedizin Berlin**  
  Campus Benjamin Franklin (CBF)  
  PI: Dr. Ulf Landmesser  
  RC: Julia Leibiger

**XIENCE 28 Global**

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  PI: Dr. Thomas Schmitz  
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- **Herzzentrum Leipzig GmbH**  
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- **Universitatsmedizin Berlin**  
  Campus Benjamin Franklin (CBF)  
  PI: Dr. Ulf Landmesser  
  RC: Julia Leibiger
Back-up slides
HBR Criteria Distribution in XIENCE 90

All Registered Patients

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 75 years</td>
<td>65.6%</td>
</tr>
<tr>
<td>Age ≥ 75 years (only)</td>
<td>35.5%</td>
</tr>
<tr>
<td>Chronic OAC therapy</td>
<td>40.8%</td>
</tr>
<tr>
<td>Anemia (Hemoglobin &lt; 11 g/dL)</td>
<td>16.2%</td>
</tr>
<tr>
<td>History of stroke</td>
<td>11.3%</td>
</tr>
<tr>
<td>CKD (creatinine ≥ 2.0 mg/dL or dialysis)</td>
<td>8.0%</td>
</tr>
<tr>
<td>Thrombocytopenia (platelet count &lt; 100,000/mm3)</td>
<td>3.0%</td>
</tr>
<tr>
<td>History of major bleeding</td>
<td>2.9%</td>
</tr>
</tbody>
</table>

Average number of criteria met: 1.5 ± 0.7
HBR Criteria Distribution in XIENCE 28

All Registered Patients

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 75 years</td>
<td>69.3%</td>
</tr>
<tr>
<td>Age ≥ 75 years (only)</td>
<td>35.1%</td>
</tr>
<tr>
<td>Chronic OAC therapy</td>
<td>43.9%</td>
</tr>
<tr>
<td>Anemia (Hemoglobin &lt; 11 g/dL)</td>
<td>15.2%</td>
</tr>
<tr>
<td>History of stroke</td>
<td>10.8%</td>
</tr>
<tr>
<td>CKD (creatinine ≥ 2.0 mg/dL or dialysis)</td>
<td>8.6%</td>
</tr>
<tr>
<td>Thrombocytopenia (platelet count &lt; 100,000/mm3)</td>
<td>3.9%</td>
</tr>
<tr>
<td>History of major bleeding</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

AVERAGE NUMBER OF CRITERIA MET: 1.6 ± 0.8
# Sample Size and Power Calculations

**Key Secondary Endpoint: BARC 2-5 Bleeding**

<table>
<thead>
<tr>
<th></th>
<th>XIENCE 90</th>
<th>XIENCE 28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>3-month clear HBR patients from XIENCE V USA</td>
<td>1-month clear HBR patients from XIENCE V USA</td>
</tr>
<tr>
<td>Hypothesis</td>
<td>Superiority for BARC 2-5 bleeding</td>
<td>Superiority for BARC 2-5 bleeding</td>
</tr>
<tr>
<td>Expected rate control</td>
<td>6.0% between 3 and 12 months</td>
<td>4.6% between 1 and at 6 months</td>
</tr>
<tr>
<td>Expected rate test</td>
<td>3.0% between 3 and 12 months</td>
<td>2.3% between 1 and 6 months</td>
</tr>
<tr>
<td>Statistical model</td>
<td>Propensity stratification</td>
<td>Propensity stratification</td>
</tr>
<tr>
<td>Test significance level ($\alpha$)</td>
<td>0.025 (1-sided)</td>
<td>0.025 (1-sided)</td>
</tr>
<tr>
<td>Attrition rate</td>
<td>15%</td>
<td>10%</td>
</tr>
<tr>
<td>Power (1-(\beta))</td>
<td>95%</td>
<td>90%</td>
</tr>
</tbody>
</table>
**Sample Size and Power Calculations**

Key Secondary Endpoint: Definite/Probable ST

<table>
<thead>
<tr>
<th></th>
<th>XIENCE 90</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Performance goal</strong></td>
<td>1.2%</td>
</tr>
<tr>
<td><strong>Statistical model</strong></td>
<td>Exact test</td>
</tr>
<tr>
<td><strong>Test significance level (α)</strong></td>
<td>0.05 (2-sided)</td>
</tr>
<tr>
<td><strong>Attrition rate</strong></td>
<td>15%</td>
</tr>
<tr>
<td><strong>Power (1-β)</strong></td>
<td>85%</td>
</tr>
<tr>
<td><strong>Sample size (N patients)</strong></td>
<td>2000</td>
</tr>
</tbody>
</table>
BARC 3-5 Bleeding Rates in HBR Trials

- **LEADERS FREE (BioFreedom arm):** 7.2%
- **LEADERS FREE II:** 7.0%
- **ZEUS:** 3.5%
- **SENIOR:** 3.0%
- **ONYX ONE (Onyx arm):** 4.9%
- **X90:** 6.4%
- **X28:** 4.6%

Bleeding BARC 3 or 5 events from 0 to 12 mos
Bleeding BARC 3-5 events from 0 to 6 mos