Patient Recruitment, Enrollment, and Retention in Clinical Trials: An Industry View

Kenneth Stein MD FACC FHRS
Senior Vice President and Chief Medical Officer
Rhythm Management and Global Health Policy
Patient Engagement in Clinical Trials

- Enrolling a Representative Population
  - WIN-Her Initiative
  - Platinum Diversity

- Patient Role in Study Design and Execution
  - Patient Members on Steering Committees
The WIN-Her™ Initiative
Women Opt In for Heart Research

Project Goals

- Understand how to overcome female enrollment barriers, especially in randomized trials
- Develop and test new enrollment approaches
- Partner with key stakeholders, including FDA, to influence dialog on this topic
- Publish and share key learnings from this effort

Key Activities

- Interviews with patients and physicians
- New types of patient education materials and site training materials
- Focus topic during regular trial conference calls
- Formal metric tracking and best practice sharing
- Screening logs to track participation data and rationale
Important Questions in Designing the WIN-Her™ Initiative

• Are there approaches that resonate better with female patients?
• How do we design an effective pilot to test new approaches?
• What materials and process are needed?
• What is the best way to engage clinical sites?
• What data is important to gather in evaluating why patients do/don’t enroll?
• How do we measure success?
WIN-Her Will Be Piloted in Two Randomized, Indication Expansion Device IDE Trials

<table>
<thead>
<tr>
<th></th>
<th>ASAP-TOO</th>
<th>MADIT-SICD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device</td>
<td>WATCHMAN™ Left Atrial Appendage Closure Device</td>
<td>Subcutaneous ICD</td>
</tr>
<tr>
<td>Candidates</td>
<td>Patients with non-valvular AF who are NOT eligible for anticoagulation</td>
<td>Post-MI diabetic patients with EF 36-50%</td>
</tr>
<tr>
<td>Goal</td>
<td>Determine whether LAAC reduces the risk of thromboembolic ischemic stroke and systemic embolism</td>
<td>Determine whether there is a survival benefit from a S-ICD</td>
</tr>
<tr>
<td>Size</td>
<td>888 patients in up to 65 global sites</td>
<td>1,400 patients in up to 80 global sites</td>
</tr>
</tbody>
</table>

WIN-Her will be conducted in US sites only (with all patients eligible for enrollment)
The WIN-Her™ Initiative Will Include New Materials for Patients and Physicians

• Patient-facing materials
  – New approach to general trial brochure (influenced by patient research)
  – Supplemental brochure specifically targeting women
  – Detailed patient website
  – Data collection questionnaire to collect perceptions about trial participation and feedback on trial materials

• Suggested talking points for physicians and coordinators
  – Patient outreach letter
  – Referring physician outreach letter
  – Patient discussion guide
  – Coordinator follow-up guide
WIN-Her Study Data Elements: Screening Log Questions

Decision Making
- Perceptions of educational materials
- Number of conversations to make a decision
- Influencers of decision
- Attitudes about clinical trials
- Reasons for NOT participating

Patient Profile
- Perception of health status
- Occupation
- Educational level
- Primary support system

Expectations of Research Participation
- Previous trial participation
- Preference of therapy received in trial
- Health expectations from trial participation

Sites will be incentivized to collect this data
WIN-Her Study Data Elements: In-Trial Data Collection

Is trial participation meeting expectations?

Why trial participation is/is not meeting expectations?
- How they are feeling healthwise compared to pre-trial
- Perception of contributions to research
- Difficulties in participations related to family/personal obligations
- Support system from friends/family related to trial participation
- Questions/concerns answered by study team
- Worries about overall health
- Transportation difficulties
Conclusions

• Enhanced patient and physician facing materials should help address known barriers to female enrollment

• Education and training related to enrollment barriers and clinical trial process will be critical

• In the pilot phase, WIN-Her Initiative will be deemed successful if 40% enrollment is female

• Data gathered from WIN-Her can inform future protocol design

• WIN-Her Initiative learnings could be potentially adapted to other geographies and cultures
PLATINUM Diversity

Enrollment: 1500 patients / 55 US sites
Primary Investigators:
  Wayne Batchelor: Florida State College of Medicine, Tallahassee
  Research Institute, & Southern Medical Group, Tallahassee, FL
  Roxana Mehran: Mount Sinai Hospital, New York, NY

≥ 1 PREMIER Stent &
one or more of the following:
• Female
• Black
• Hispanic/Latino
• American Indian or Alaskan Native

Follow-up (telephone):
• 30 days
• 6 months
• 1 year

Primary Endpoint:
• 12M Death/MI/TVR

• Women and minorities are vastly underrepresented in cardiac clinical trials
• First of its kind study of women and minorities with coronary stents
• Sociodemographic, clinical and procedural data were collected
• Enrollment completed Aug 13, 2015..... 6 months ahead of schedule!
• Selection of sites treating diverse patient population was the most important
  factor in rapid enrollment and success of study
### Diverse enrollment tactics

- Selection of sites serving a diverse patient population
- Medical affairs feedback on cath lab demographics
- CTG strategic partner feedback
- CRO and PI training

### Close the Gap Strategic Partners

- Association of Black Cardiologists
- Womenheart
- Society for Cardiac Angiography and Intervention-Women in Innovation (SCAI-WIN)
- National Medical Association
- National Minority Quality Forum
- National Forum for Heart Disease and Stroke Prevention
## Site Scorecard

### Project: EVOLVE II

<table>
<thead>
<tr>
<th>SITE</th>
<th>CENTER CODE</th>
<th>INVESTIGATOR</th>
<th>LOCATION</th>
<th>ACTIVATION DATE</th>
<th>PATIENTS ENROLLED</th>
<th>FEMALE SHARE OF ENROLLMENT</th>
<th>NON-WHITE SHARE OF ENROLLMENT</th>
</tr>
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<tbody>
<tr>
<td>Turku University Hospital</td>
<td>504</td>
<td>Airaksinen, Juhani</td>
<td>Finland</td>
<td>06-Mar-2013</td>
<td>29</td>
<td>17.2%</td>
<td>0.0%</td>
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<tr>
<td>University of Miami Hospital</td>
<td>1342</td>
<td>Alfonso, Carlos</td>
<td>United States</td>
<td>19-Apr-2013</td>
<td>6</td>
<td>33.3%</td>
<td>66.7%</td>
</tr>
<tr>
<td>Kokura Memorial Hospital</td>
<td>1634</td>
<td>Ando, Kenji</td>
<td>Japan</td>
<td>13-Dec-2012</td>
<td>20</td>
<td>35.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>St. Vincent’s Hospital</td>
<td>111</td>
<td>Ball, Michael</td>
<td>United States</td>
<td>25-Jan-2013</td>
<td>23</td>
<td>17.4%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Tallahassee Memorial Hospital</td>
<td>947</td>
<td>Batchelor, Wayne</td>
<td>United States</td>
<td>19-Dec-2012</td>
<td>24</td>
<td>45.8%</td>
<td>20.8%</td>
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<tr>
<td>North Colorado Medical Center</td>
<td>1935</td>
<td>Beckmann, James</td>
<td>United States</td>
<td>24-Apr-2013</td>
<td>1</td>
<td>100.0%</td>
<td>0.0%</td>
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<tr>
<td>Clinique Saint-Hilaire Rouen</td>
<td>263</td>
<td>Berland, Jacques</td>
<td>France</td>
<td>04-Jul-2013</td>
<td>17</td>
<td>11.8%</td>
<td>100.0%</td>
</tr>
<tr>
<td>North Mississippi Medical Center</td>
<td>102</td>
<td>Bertolet, Barry</td>
<td>United States</td>
<td>28-Feb-2013</td>
<td>22</td>
<td>18.2%</td>
<td>4.5%</td>
</tr>
<tr>
<td>Geisinger Medical Center</td>
<td>168</td>
<td>Blankenship, James</td>
<td>United States</td>
<td>02-May-2013</td>
<td>17</td>
<td>35.3%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Baptist Medical Center Princeton</td>
<td>103</td>
<td>Bouchard, Alain</td>
<td>United States</td>
<td>28-Feb-2013</td>
<td>31</td>
<td>48.4%</td>
<td>19.4%</td>
</tr>
</tbody>
</table>
Conclusions

• Women showed an increased risk of death/MI vs Men

• Minorities showed an increased risk of MI and death/MI vs Whites

• Similar rates of TVR and ST among all 3 groups suggest that “device failure” is unlikely to account for the observed differences

• These results highlight the heterogeneity conferred by sex and race and suggest further study into the biologic, social, behavioral, and economic factors that impact CV risk after DES
Why Add a Patient to a Steering Committee?

• Clinical trial designs need to become more patient-centric
  – Do the study endpoints measure something that is meaningful to the patient?
  – Education and associated materials: Are patient materials (e.g. informed consent, study brochures) clear and relevant?
  – Participation: Impact of participating in the trial on patients (time commitment, travel, expenses, interventions): Is the trial unduly burdensome
Defining Expectations

• Patient Profile
  – Prefer that the patient have the specific condition being studied

• Patient Selection
  – Solicited nominations from study PI (or other steering committee members)

• Steering Committee Services & Duration of Participation
  – Patient advisor is a “full-fledged” steering committee member

• Payment Definition
  – Worked with legal to define payment terms and fair market value for participation
Success Stories! SMART MSP

- Patient representative is an RN
- Travelled to participate in steering committee meeting concurrent with HRS
- Provided important feedback on informed consent forms and burden of testing

Lessons Learned:
- Steering committee members struggled to identify patients
- Ensure that patient advisor is willing to travel for occasional meetings. BSC covers travel costs. Currently BSC HCP travel guidelines are applied to patient representatives.
Success Stories! SMART CRT

• Patient steering committee member participated in in-person steering committee meeting in Nov 2016
  – Engaged in the meeting discussion and provided meaningful feedback on how the required study design/visits may impact patient participation
• Provided the team with patient-centric feedback on protocol and informed consent
  – Specifically, he asked for the consent form to be greatly reduced (with minimal legal jargon) with a possible video component
• Amended contract in March 2017 to allow patient to participate in AdvaMed Patient Engagement Event – very positive response to his participation in this event
Patient Engagement in Clinical Trials

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  – Win-HER initiative
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