On-X heart valves | a product group of On-X Life Technologies, Inc.™

On-X Heart Valve: Lowered Anticoagulation Trial

The On-X® prosthetic heart valve continues to demonstrate tolerance of low INR that has been seen in worldwide studies.

The On-X Heart Valve:

FDA approved in 2001

17 years of clinical excellence

Proven exceptional patient results

Prospective Randomized On-X Anticoagulation Clinical Trial (PROACT): FDA application submitted to lower INR levels for On-X valve patients.

On-X® Standard Aortic Prosthetic Heart Valve

October 2012: On-X Life Technologies, Inc.™ submitted applications to the U.S. FDA and to the Conformité Européenne (CE) for revised Instructions for Use (IFU) recommending lower INR levels (1.5 – 2.0) for patients with On-X aortic valves. The applications were submitted based upon the results of the PROACT high-risk aortic valve patient group.

If the IFU changes are approved, the On-X valve will become the first mechanical aortic heart valve that may be maintained at these lower INR levels.

PROACT Test Groups[1-3]

Pre-randomization

Transition Period
First three postoperative months with standard anticoagulation therapy[3]

AVR = aortic valve replacement
MVR = mitral valve replacement

Post-randomization

Low Risk AVR
After loading dose, Clopidogrel 75 mg/day, Aspirin 325 mg/day

High Risk AVR
INR 1.5 to 2.0, Aspirin 81 mg/day

All MVR
INR 2.0 to 2.5, Aspirin 81 mg/day

Control Groups
Each of the three post-randomization groups will be given standard anticoagulation therapy[3]

PROACT Patient Group Criteria

PROACT Trial High Risk AVR Criteria

- Chronic atrial fibrillation
- Left ventricular ejection fraction < 30%
- Enlarged left atrium > 50mm diameter
- Spontaneous echo contrasts in the left atrium
- Neurological events (any history prior stroke or TIA)
- Left or right ventricular aneurysm
- Women receiving estrogen replacement therapy
- Hypercoagulability

PROACT Trial Low Risk AVR Criteria

Patients are considered low risk only if they have no high risk factors.

PROACT Trial Exclusion Criteria

- Multiple valve replacement (MV repair is acceptable)
- Active endocarditis
- Terminal illness
- Emergency cases
- Inability to return for follow-up
- Persons unable to give adequate consent

Clinicians Discuss the PROACT Trial

The On-X valve represents a paradigm shift in how we care for patients with valve disease. As a direct result of its advanced materials and engineering design, a lower level of anticoagulation seems possible for On-X valves based on the preliminary results of the PROACT trial. If these are confirmed at the conclusion of this seminal trial,

"This is a truly remarkable advance in mechanical valves, and this story needs to be shared more within our cardiac community."

certain On-X patients may be treated with aspirin and clopidrogel and others will be treated to much lower than traditional INR targets on warfarin. The ultimate benefit to be derived for On-X valve patients will be reduced bleeding events without engendering increased thromboembolic risk. This is a truly remarkable advance in mechanical valves, and this story needs to be shared more within our cardiac community.

Mohan Sathyamoorthy, M.D., F.A.C.C., Vice Chief, Cardiovascular Division, Baylor All Saints Medical Center, Fort Worth, TX, Assistant Clinical Professor of Medicine, Adjunct Faculty, Department of Medicine, Division of Cardiovascular Medicine, Vanderbilt University

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"The On-X valve may be the next step in the evolution of valve technology. Traditionally, older patients would receive tissue valves to avoid the bleeding risk associated with taking higher levels of Coumadin. However, when tissue valve patients live into their 80s and 90s, they run the risk of having replacement surgery in eight to 16 years when the tissue valve wears out.

"The On-X valve may be the next step in the evolution of valve technology..."

This FDA study has the potential for changing our choices in heart valves in the future. If we can show that it is safe to use a mechanical valve with low levels of Coumadin or alternative drugs that are safe—or even no Coumadin—the choice in these borderline older patients will be completely different."

Hillel Laks, M.D., University of California Los Angeles School of Medicine, Department of Cardiothoracic Surgery

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"The 'holy grail' for cardiac surgeons implanting heart valves has been 'A Valve for Life'," If the approved FDA reduced anticoagulation study is successful, the On-X valve will become the

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safe valve of choice for a new generation of patients who are expected to enjoy a long life, and we will finally approach the concept of 'A Valve for Life'."

Sidney Levitsky, M.D., Cheever Professor of Surgery at Harvard Medical School and Director of Cardiothoracic Surgery for CARE Group, Boston, Mass., and chair of the Reduced Anticoagulation Clinical Trial of the On-X Prosthetic Heart Valve Data Safety Monitoring Committee.

On-X Valve Lowered Anticoagulation Trial

2001
On-X Valve FDA approved

2006
Exceptional worldwide On-X valve clinical data results inspired PROACT Trial

2006
PROACT Trial initiated

2011
Positive preliminary results presented at American College of Cardiology (ACC) Annual Meeting[4]

2012
Submission to FDA for IFU changes for high-risk aortic group

2013
Projected submission to FDA for IFU changes for low-risk group

2014
Projected submission to FDA for IFU changes for mitral group

1. FDA Approved Non-Warfarin and Reduced Warfarin Anticoagulation Trial of the On-X Prosthetic Heart Valve Initiated at Emory Crawford Long Hospital -Tuesday, August 22, 2006. News release Medical Carbon Research Institute, LLC, Austin, Texas USA; © 2006 http://www.onxvalves.com/about_news_item.asp?NewsID=31
2. PROACT Investigation Plan. Medical Carbon Research Institute, LLC, Austin,Texas USA; © 2006
3. ACC/ AHA 2006 Guidelines for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the1998 Guidelines for the Management of Patients With Valvular Heart Disease): Developed in Collaboration With the Society of Cardiovascular Anesthesiologists Endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons Circulation 2006;114;84-231. DOI: 10.1161/CIRCULATIONAHA.106.176857.
4. Puskas JD, Quinn R, Fermin L, McGrath M, Gerdisch M, Hughes C, Martin T, Kong B, Nichols D. Reduced anticoagulation for a mechanical heart valve. Presented at the American College of Cardiology 2011, New Orleans, Louisiana, USA, April 4, 2011 in Late-Breaking Clinical Trials

On-X aortic and mitral valves are FDA approved.

Until the PROACT Trial is complete, On-X Life Technologies recommends all patients should be retained on existing ACC/AHA guidelines for mechanical valve anticoagulation. CAUTION: Federal law restricts this device to sale by or on the order of a physician. Refer to the Instructions for Use that accompany each valve for indications, contraindications, warnings, precautions and possible complications. CAUTION: This investigational use of this device is limited by Federal law to investigational sites. For further information, visit www.onxlti.com.

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