New Lantheus Study Finds Significant Survival Benefit for Critically Ill Patients Undergoing Contrast-Enhanced Echocardiography

March 29, 2009 3:04 PM ET

Data Presented at the American College of Cardiology's 58th Annual Scientific Session
Reinforce Benefit/Risk Profile of Cardiac Ultrasound Contrast Use

N. BILLERICA, Mass. (March 29, 2009) – Lantheus Medical Imaging, Inc., a worldwide leader in diagnostic imaging, today announces new data regarding the use of DEFINITY® Vial For (Perflutren Lipid Microsphere) Injectable Suspension. A large, retrospective study (abstract number 1027-265) presented by Dr. Michael Main at the 58th Annual Scientific Sessions of the American College of Cardiology held in Orlando, Florida, demonstrated that use of contrast-enhanced echocardiography was associated with a significantly improved short-term survival among critically ill, intensive care unit (ICU) patients, when compared with matched patients receiving non-contrast echocardiography. Patients who received contrast exhibited a 26 percent lower risk of short-term mortality within 48 hours after the exam when compared with patients who received echocardiography without the ultrasound contrast agent. Transthoracic echocardiography, the most common type of echocardiogram, uses a transducer on a person's chest to send high frequency ultrasound waves through the chest wall to the heart to create pictures of the heart that physicians can then analyze.[1] DEFINITY® is used to improve the images of suboptimal non-contrast echocardiograms.

These findings build on a recent multicenter retrospective study of over 4 million hospitalized patients published in the *American Journal of Cardiology* that also demonstrated that echocardiography with DEFINITY® was associated with a lower risk of short-term mortality in comparison with patients undergoing non-DEFINITY® echocardiograms (Main et al, *American Journal of Cardiology*, Volume 102, Issue 12, 2008).

"The data demonstrate a significantly lower risk of short-term mortality among critically ill patients receiving contrast-enhanced echocardiograms and affirm the clinical value of echocardiogram contrast agents as an important diagnostic tool for specialized patient populations," said Michael L. Main, M.D., associate professor of medicine, University of Missouri, Kansas City, director, Echocardiography Laboratory, Saint Luke's Mid America Heart Institute, Kansas City, Missouri, and lead author on the study. "Given the limited diagnostic options for critically ill patients, we are encouraged by these results that demonstrate the survival benefit of contrast-enhanced echocardiograms in an ICU setting."

Using the Premier Perspective™ database, 145,882 adult inpatient records were matched by propensity score for age, race, gender, hospital and admission type, multiple co-morbid conditions and APR-DRG severity of illness. Of these, 39,189 patients were critically ill and in the ICU when the echocardiogram was performed, 19,318 patients received contrast-enhanced studies, approximately 78 percent of the total population received DEFINITY®. A subset of 12,572 patients on mechanical ventilation was also examined.

Short-term mortality rates (<48 hours of echocardiogram) were 2.98 percent for patients undergoing non-contrast studies and 2.30 percent for patients undergoing contrast-enhanced examinations. A multivariate logistic regression analysis was used to compare short-term mortality, controlling for case mix and clinical covariates. Critically ill patients undergoing contrast-enhanced echocardiograms had a statistically significant 26 percent lower risk-adjusted odds ratio for 48-hour mortality than those patients who received only echocardiography without the ultrasound contrast agent. For those patients on mechanical ventilation, 48-hour mortality rates were 6.11 percent for those undergoing non-contrast exams and 4.59 percent for individuals with contrast-enhanced examinations, representing a 27 percent lower mortality rate for the contrast-enhanced group.

"With DEFINITY® already widely used in the intensive care unit settings, the results confirm that there is a survival advantage associated with using echocardiogram contrast agents appropriately," said Mark Hibberd, M.D., Ph.D., senior medical director, Global Medical Affairs, Lantheus Medical Imaging, Inc. and co-author on the study. "The contrast-associated survival advantage is important, especially in the mechanically ventilated patients, in whom routine echocardiography without contrast is especially challenging. The current database analysis does not allow us to draw conclusions on the reasons why contrast utilization is associated with a survival advantage. Some possible explanations include more accurate, faster diagnoses leading to better patient management decisions, and/or the avoidance of other potentially higher-risk or invasive tests that become unnecessary after contrast echocardiography. This study follows the recent publication of a prospective study by Kurt et al (*Journal of the American College of Cardiology*, Volume 53, Issue 9, March 3, 2009) in which it was demonstrated that echocardiogram image quality was significantly improved in 88 percent of those studies having suboptimal images without contrast and where the

use of DEFINITY® significantly changed patient management particularly in ICU/SICU patients. The Kurt et al study gives the medical community further clinical evidence of the important role DEFINITY® can play in improving the standard of care for patients in the ICU."

About DEFINITY®

Since its launch in 2001, activated DEFINITY® Vial For (Perflutren Lipid Microsphere) Injectable Suspension has been administered to over two million patients.[2] In patients with suboptimal echocardiograms, DEFINITY® enables physicians to visualize the borders of the heart more clearly.[3,4]

In 2008, Lantheus announced the initiation of CaRES (**C**ontrast Echoc**a**rdiography **RE**gistry for **S**afety Surveillance), the first multi-center Phase IV observational registry that will further evaluate the safety profile of DEFINITY® in patients with suboptimal echocardiograms and provide safety information on the use of ultrasound contrast agents in routine clinical practice. The open-label, non-randomized registry is being conducted in more than 10 clinical sites in the United States and will include at least 1,000 patients. The study will gather data on patient characteristics and demographics, indication for DEFINITY®'s use, results of safety monitoring of patients during and after DEFINITY® administration, and the nature and frequency of any adverse events that may occur.

Indications

Activated DEFINITY® (Perflutren Lipid Microsphere) Injectable Suspension is indicated for use in patients with suboptimal echocardiograms to opacify the left ventricular chamber and to improve the delineation of the left ventricular endocardial border. The safety and efficacy of DEFINITY® with exercise stress or pharmacologic stress testing have not been established. For full prescribing information, please visit www.lantheus.com.

Important Safety Information About DEFINITY®

WARNING: Serious Cardiopulmonary Reactions

Serious cardiopulmonary reactions, including fatalities, have occurred during or following perflutren-containing microsphere administration.

- Assess all patients for the presence of any condition that precludes DEFINITY® administration (see CONTRAINDICATIONS).
- In patients with pulmonary hypertension or unstable cardiopulmonary conditions, monitor vital sign measurements, electrocardiography and cutaneous oxygen saturation during and for at least 30 minutes after DEFINITY® administration (see WARNINGS).
- **Always have resuscitation equipment and trained personnel readily available.**

Do not administer DEFINITY® to patients with known or suspected cardiac shunts (right-to-left, bi-directional or transient right-to-left), or hypersensitivity to perflutren. Do not administer DEFINITY® by intra-arterial injection.
In postmarketing use, uncommon but serious reactions observed during or shortly following perflutren-containing microsphere administration included fatal cardiac or respiratory arrest, loss of consciousness, convulsions, symptomatic arrhythmias (atrial fibrillation, supraventricular tachycardia, ventricular tachycardia or fibrillation), hypotension, respiratory distress or cardiac ischemia (see ADVERSE REACTIONS). The risk for these reactions may be increased among patients with pulmonary hypertension or unstable cardiopulmonary conditions (acute myocardial infarction, acute coronary artery syndromes, worsening or unstable congestive heart failure, serious ventricular arrhythmias or respiratory failure, including patients receiving mechanical ventilation). In the absence of these underlying conditions, observe patients closely during and following DEFINITY®

administration.
Always have cardiopulmonary resuscitation personnel and equipment readily available prior to DEFINITY® administration and monitor all patients for acute reactions.

About Lantheus Medical Imaging, Inc.

Lantheus Medical Imaging, Inc., a worldwide leader in diagnostic medicine for the past 50 years, is committed to advancing the field of diagnostic imaging. The company's proven success in discovering, developing and marketing innovative medical imaging agents provides an unparalleled platform from which to bring forward breakthrough new tools for the diagnosis and management of disease. The company is home to leading diagnostic imaging brands, including Cardiolite® (Kit for the Preparation of Technetium Tc99m Sestamibi for Injection), DEFINITY® Vial For (Perflutren Lipid Microsphere) Injectable Suspension, and TechneLite® (Technetium Tc99m Generator) and has nearly 700 employees worldwide with headquarters in North Billerica, Massachusetts, and offices in Puerto Rico, Canada, and Australia. For more information, visit www.lantheus.com.

[1] National Institutes of Health. National Heart, Lung, and Blood Institute. What is Echocardiography? http://www.nhlbi.nih.gov/health/dci/Diseases/echo/echo_all.html

[2] Source: *The Echocardiography Monthly Monitor: United States, October 2001-September 2007*, Arlington Medical Resources, Inc., Malvern, PA.

[3] Kitzman DW et al. Efficacy and safety of the novel ultrasound contrast agent perflutren (definity) in patients with suboptimal baseline left ventricular echocardiographic images. *AM J Cardiol.* 2000; 86: 669-674.

[4] Data on file, Lantheus Medical Imaging, Inc.