

New Study Published in *The American Journal Of Cardiology* Finds Survival Benefit Among Hospitalized Patients Undergoing Definity®-Enhanced Echocardiography

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Multicenter Study Results Find No Difference in Acute Mortality Rates for Patients Undergoing Contrast versus Non-Contrast Echocardiograms

N. BILLERICA, Mass. (December 15, 2008) – Lantheus Medical Imaging, Inc. a worldwide leader in diagnostic imaging, announced today new data from a retrospective, multicenter, cohort study of over four million hospitalized patients that shows similar unadjusted mortality rates for patients receiving DEFINITY® Vial For (Perflutren Lipid Microsphere) Injectable Suspension enhanced resting echocardiography exams when compared with patients who did not receive DEFINITY®. Although the patients that received DEFINITY® were sicker on average and had a higher baseline mortality risk prior to the exam, following DEFINITY® administration these same patients exhibited a 24% reduced risk of mortality over 24 hours compared to the those patients who received only echocardiography without the ultrasound contrast agent. These study findings were published in the December 2008 issue of *The American Journal of Cardiology*.

“As the largest retrospective, observational study to date to examine the short-term safety profile of perflutren-containing ultrasound contrast agents, the data highlight the relatively low incidence of adverse safety reactions associated with DEFINITY® and demonstrate a significantly lower risk of acute mortality for patients receiving DEFINITY®-enhanced echocardiograms,” said Mark Hibberd, M.D., Ph.D., Senior Medical Director, Global Medical Affairs, Lantheus Medical Imaging, Inc. and co-author on the study. “These study findings provide the physician community with essential safety information on the use of DEFINITY®, especially among hospitalized patients, and provide valuable information on patient outcomes that bear further investigation.”

The study was designed to assess short-term (one-day) mortality in hospitalized patients undergoing resting transthoracic echocardiography both with and without DEFINITY®. The study analyzed more than 4.3 million patients undergoing clinically indicated echocardiography from January 1, 2002 through October 31, 2007 using the Premier Perspective Database, the largest U.S. hospital-based, service-level comparative database providing detailed resource utilization data along with patients’ primary and secondary diagnosis and procedure codes. Of this population, 4,242,712 patients received non-enhanced echocardiograms and 58,254 received contrast-enhanced studies using DEFINITY®.

One-day mortality rates were 1.08% for patients undergoing non-contrast studies and 1.06% for patients undergoing DEFINITY® contrast-enhanced examinations. However, patients receiving DEFINITY® were more likely to have an increased baseline severity of illness and a higher pre-study risk of mortality. A multivariate logistic regression analysis was used to compare 24-hour mortality, controlling for case mix and clinical covariates. Patients undergoing DEFINITY® -enhanced echocardiograms had a 24% lower risk adjusted odds ratio for mortality within one day than those patients who received only echocardiography without the ultrasound contrast agent.

These findings build on and corroborate a recently published multicenter retrospective study that also demonstrated no increased mortality in patients undergoing echocardiography with a contrast agent in comparison with patients undergoing non-contrast-enhanced examinations (*Journal of the American College of Cardiology*, Volume 51, Number 17, 2008).ⁱ In addition, this multicenter analysis was presented in part at a meeting of the United States Food and Drug Administration Cardiovascular and Renal Drugs Advisory Committee in June, 2008.

These study findings also confirm the safety profile of ultrasound contrast imaging agents and support the implementation of the recently published American Society of Echocardiography (ASE) Consensus Statement on the Clinical applications of Ultrasound Contrast Agents in echocardiography.

“This study is groundbreaking in the echocardiography area, and represents the largest evaluation of resting echocardiography among hospitalized patients,” continued Dr. Hibberd of Lantheus. “It is also the first to evaluate the impact of contrast echocardiography on survival among hospitalized patients. The results clearly indicate that there is no additional risk associated with DEFINITY®-enhanced studies, while in fact those patients that received DEFINITY® had improved short-term survival when compared to those who received only transthoracic echocardiograms without DEFINITY®. The study did not address the reason for this effect. These data provide the medical community with further clinical evidence of how DEFINITY® can significantly improve the standard of care for patients undergoing cardiac evaluations, and we are continuing to explore the role of

DEFINITY® in specialized patient populations such as those in the ICU and receiving mechanical ventilation."

Don Kiepert, President and CEO, Lantheus Medical Imaging added, "We are encouraged by these data that further demonstrate the role and clinical value of DEFINITY®, and believe these findings will answer any remaining safety questions regarding ultrasound contrast agents. Lantheus continues to remain committed to providing important safety information on the use of DEFINITY® in routine clinical practice."

About DEFINITY®

Since its launch in 2001, activated DEFINITY® Vial For (Perflutren Lipid Microsphere) Injectable Suspension has been administered to over two million patients.ⁱⁱ In patients with suboptimal echocardiograms, DEFINITY® enables physicians to visualize the borders of the heart more clearly.^{iii,iv}

In May 2008, Lantheus announced the initiation of CaRES (Contrast Echocardiography REgistry for Safety 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 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.

Important Safety Information about DEFINITY®

Activated DEFINITY® Vial for (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.

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.**

Activated DEFINITY® should not be administered 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.

For full prescribing information, please visit www.lantheus.com.

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.

ⁱ Wei K, et al. The safety of definity and optison for ultrasound image enhancement: a retrospective analysis of 78,353 administered contrast doses. *J Am Coll Cardiol*;51(17):1202-1206.

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

ⁱⁱⁱ 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.

^{iv} Data on file, Lantheus Medical Imaging, Inc

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