AUTOPULSE SYSTEM

Preliminary Findings Reported from the CIRC Trial

On January 11, 2011, enrollment in the Circulation Improving Resuscitation Care (CIRC) trial successfully closed as it became the first large-scale randomized resuscitation trial to reach a statistically significant result. Preliminary findings strongly confirm that the AutoPulse® Non-invasive Cardiac Support Pump is both safe and efficacious when used for cardiac arrest patients.

A Successful Landmark Trial

The CIRC trial succeeded where other trials failed in its reaching a meaningful endpoint. In contrast, other resuscitation trials, such as those that looked at the use of hypertonic saline and the impedance threshold device, were terminated for futility (i.e., additional patients would not produce a statistically valid answer).

A Uniquely Designed Trial

The CIRC trial compared the rates of survival to hospital discharge from out-of-hospital cardiac arrest patients treated with the load-distributing band AutoPulse to those receiving manual CPR. The trial began in 2007 and enrolled in excess of 4,000 patients. It was governed by an independent Data Safety Monitoring Board that reviewed interim outcome and safety data on seven separate occasions.

The CIRC trial employed a *Sequential Triangular* design. Modeled after larger drug trials, it is designed to deliver a definitive answer. This design is rarely attempted since it requires many more patients[1] and is more expensive to conduct.

Whether the result proved to be better, worse, or equal, the design delivers findings are statistically significant. Attainment of a definitive result is important. Findings of "no difference" or "futility" do not prove anything, and, in fact, leave open the possibility that the tested therapy could be worse for the patient.

A Focus on Uniform Competence of Manual CPR

To reduce any bias from poorly performed manual CPR that would favor the AutoPulse and address questions left open from earlier trials, care was taken to ensure that the manual CPR in the control arm was performed with uniform competence. In particular, there was a focus on minimizing "hands off" time throughout the trial.

At the start of the trial, each of the participating 5,000 medics received refresher training and was required to demonstrate proficiency in manual CPR. Over the course of the trial, they were retrained and were required to demonstrate proficiency to a predetermined level at six-month intervals. Sites had to maintain their aggregate CPR Fraction[2] above minimal thresholds to continue enrolling patients. Specifics of the CIRC trial design have been published.[3]

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AutoPulse is Safe and Effective

The preliminary results of the CIRC trial confirm the important role the AutoPulse system plays in improving resuscitation. The trial unequivocally removes any lingering doubt about its safety and efficacy by demonstrating equivalence to an American Heart Association (AHA) recommended Class I intervention.

Equal is a Strong Outcome for the CIRC Trial

The CIRC trial's preliminary finding is especially significant since the control arm of the trial produced a level of manual CPR that agencies are not typically staffed or resourced to deliver. Protocol compliance monitoring shows that the CIRC sites had CPR Fractions approaching 85 percent. This was 23 percent higher than the value previously reported from a well-designed trial conducted by the Research Outcomes Consortium.

An Answer for the Guidelines

The AHA's 2010 *Guidelines*, and to a similar extent the European Resuscitation Council (ERC) Guidelines, concluded that more research was needed before a recommendation could be made for the routine use of load-distributing band devices such as the AutoPulse. These findings definitively answer the call for additional information. If the CIRC findings had been available, ZOLL believes that the recommendation would have been upgraded.

A Milestone in Resuscitation

When the CIRC trial's findings are published, they will mark a milestone in resuscitation research for both their conclusions and the quality of the trial design. It will be some time before the complete picture unfolds. At the close of enrollment, there were still more than 400 patients whose follow-up was not complete. Months of effort is required to finalize the database and perform the many sub-analyses. Nonetheless, these preliminary findings make it clear that the AutoPulse is an important part of improving resuscitative efforts.

[1] B Rosner. *Fundamentals of Biostatistics (6th edition)*. Thomson Higher Education.2006;697.

[2] Percentage of the CPR interval during which compressions are delivered.

[3] EB Lerner et al. Design of the Circulation Improving Resuscitation Care (CIRC) trial: a new state of the art design for out-of-hospital cardiac arrest research. *Resuscitation*. 2010;doi:10.1016/j.resuscitation.2010.11.013.

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Printed in the U.S.A. PN-179 011105

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