

Commenting on the differences between the ALPHA OMEGA Trial and earlier trials, Luigi Tavazzi, MD, Villa Maria Cecilia Hospital, Cotignola, Italy, noted three factors that may have influenced the results: the relatively small sample size, the low dose of EPA-DHA, and whether the components of the composite primary endpoint were specific enough for the specific mechanisms of action of n-3 fatty acids. Of note, the endpoints in question were based on previous prospective cohort studies that demonstrated that n-3 fatty acids lowered the risk of coronary heart disease as well as stroke. While praising the investigators for attempting the trial, Prof. Tavazzi pointed out that clinicians should use caution when using the ALPHA OMEGA Trial results to draw conclusions about the effect of n-3 fatty acids in this studied population.

Results of the ALPHA OMEGA Trial were published online in *the New England Journal of Medicine* at NEJM.org (10.1056/NEJMoa1003603).

## Stem Cell Transplantation Improves Heart Function and Survival in Chronic Heart Failure

Injecting autologous stem cells directly into the hearts of patients with heart failure improves hemodynamic function, quality of life, and survival, according to new results from the STAR Heart study. The open-label, nonrandomized study is the largest trial to date that has compared stem cell transplantation with standard therapy for patients with chronic heart failure due to ischemic heart disease.

The STAR Heart study included 391 patients with chronic heart failure, defined as a left ventricular ejection fraction (LVEF)  $\leq 35\%$ . All patients experienced myocardial infarction (MI) that was treated by percutaneous coronary intervention (PCI) for a mean of 8.5 years prior to study enrollment. A total of 191 patients agreed to undergo treatment with autologous stem cell transplantation, and the remaining 200 patients acted as controls. All patients were also receiving optimal medical therapy for heart failure.

The transplant procedure involved harvesting autologous stem cells from the bone marrow and delivering these cells (mean, 66 million) directly into the area of ischemic damage via intracoronary balloon catheter. Patients were examined at 3 months, 12 months, and 5 years after transplantation. Dr. Bodo-Eckehard Strauer, Heinrich-Heine-University of Duesseldorf, Duesseldorf, Germany, reported long-term results from the study.

Within 3 months, patients in the transplant group showed improvements in LV performance compared with

baseline, including a 22% improvement in cardiac index ( $p < 0.01$ ), 15.4% increase in exercise capacity ( $p < 0.01$ ), 11% increase in peak oxygen uptake ( $p < 0.05$ ), and 6.3% increase in oxygen pulse ( $p < 0.05$ ). LVEF also increased by 22.4%, from 29.4% at baseline to 36% at 3 months ( $p < 0.01$ ). By comparison, all hemodynamic parameters worsened in the control group, including a 0.5% absolute reduction in LVEF ( $p < 0.05$ ).

Patients in the transplant group sustained significant improvements in all measures of hemodynamics, exercise capacity, LV contractility, and LV geometry through the 5-year follow-up period. This included a 25.1% increase in LVEF ( $p < 0.01$ ), a 4.9% reduction in end diastolic volume ( $p < 0.5$ ), a 13.7% reduction in end systolic volume ( $p < 0.01$ ), and a 15.1% increase in shortening velocity ( $p < 0.01$ ). Patients in the control group showed a significant deterioration in each of these measures from baseline to 5 years ( $p < 0.05$  for all) despite optimal medical therapy.

Improvements in LV performance were associated with prolonged survival among stem cell recipients. At 5 years, 184 of 191 patients were alive in the transplant group, compared with 168 of 199 control patients ( $p < 0.01$ ). Overall, these findings suggest a promising role for autologous stem cell transplantation in improving cardiac function and survival among patients with ischemic cardiomyopathy.

## Ivabradine Added to Standard Therapy Improves Outcomes In Patients With Systolic HF

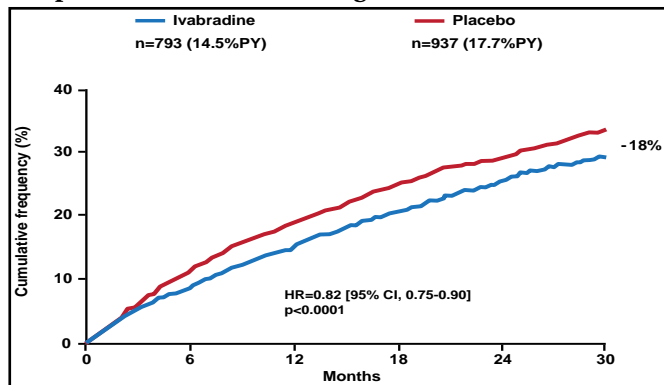
In patients with chronic heart failure (HF), elevated resting heart rate (HR) is a risk factor for adverse outcomes [Fosbøl EL et al. *Int J Cardiol* 2010]. Results of the Systolic Heart Failure Treatment with the *If* Inhibitor Ivabradine Trial (SHIFT; ISRCTN70429960), presented by Michel Komajda, MD, La Pitié-Salpêtrière Hospital, Paris, France, indicate that when added to standard therapy, ivabradine reduced HR (Figure 1) and improved outcomes in subjects with systolic HF as early as 3 months [Swedberg K et al. *Lancet* 2010].

All subjects had NYHA class II to IV HF, left ventricular ejection fraction  $\leq 35\%$ , and resting HR  $\geq 70$  beats per minute (bpm); received recommended HF therapy ( $\sim 90\%$  on  $\beta$ -blockers; 56% at target daily dose); and had been hospitalized for worsening HF within the previous 12 months. Participants were randomly assigned to receive either ivabradine ( $n = 3241$ ; 5 mg bid, titrated to a maximum of 7.5 mg based on HR and tolerability) or placebo ( $n = 3264$ ). The primary outcome measure

was a composite of cardiovascular (CV) mortality and hospitalization for worsening HF.

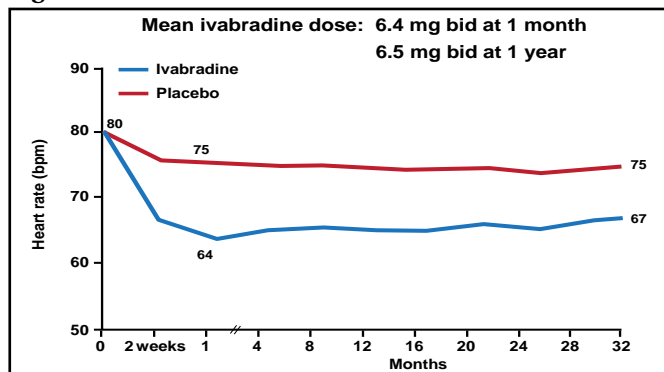
Median follow-up was 22.9 months. There was an 18% relative risk reduction [RRR] (absolute risk reduction of 4.2%) for the primary endpoint in patients who received ivabradine (HR, 0.82; 95% CI, 0.75 to 0.90;  $p < 0.0001$ ; Figure 1). The beneficial effect of ivabradine was driven mainly by a 26% RRR in hospitalizations for HF (HR, 0.74; 95% CI, 0.66 to 0.83;  $p < 0.0001$ ). Results were consistent among subjects, except that subjects with baseline HR  $\geq 77$  bpm had a greater reduction in the primary endpoint with ivabradine ( $p = 0.029$ ; Figure 2).

**Figure 1. Primary Endpoint: Cardiovascular Mortality/Hospitalization for Worsening HF.**



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**Figure 2. Mean Heart Rate Reduction.**



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Deaths due to HF were significantly lower in subjects who received ivabradine versus placebo (HR, 0.74; 95% CI, 0.58 to 0.94;  $p = 0.014$ ). Although there were fewer CV (HR, 0.91; 95% CI, 0.80 to 1.03) and all-cause deaths (HR, 0.90; 95% CI, 0.80 to 1.02) in the ivabradine group, the differences were not significant ( $p = 0.128$  and  $p = 0.092$ , respectively). There was a modest but significant ( $p = 0.0003$ ) improvement in NYHA class in the ivabradine group. Ivabradine was safe and well tolerated.

## Bilateral Versus Single Internal Mammary CABG: One-Year Results from the ART Trial

The use of bilateral internal mammary artery (BIMA) grafting is safe according to one-year data from the Arterial Revascularization Trial (ART). David P Taggart, MD, PhD, Professor of Cardiovascular Medicine, University of Oxford and John Radcliffe Hospital, Oxford, UK, presented findings from the one-year analysis of ART, a large international, multicenter, randomized clinical trial of 3102 patients comparing the use of bilateral versus single internal mammary artery grafting in coronary artery bypass grafting (CABG) patients. The study is the largest randomized trial of two surgical procedures ever undertaken in cardiac surgery and is funded for 10 years to determine whether or not BIMA reduces long-term mortality and the need for repeat revascularization. One-year analyses focused on the safety and feasibility of this interventional approach.

For the overall study, the primary endpoint is survival at 10 years and the secondary endpoints include 30 day and cause specific mortality, the need for revascularization, clinical events, quality of life measures, and cost-effectiveness measures. Follow-up analysis at one year included 3069 patients who were randomized to either single internal mammary artery (SIMA) grafting (n=1540) or BIMA (n=1529). Patients were well-matched at baseline. The use of BIMA increased the mean surgery length by 23 minutes and the mean ventilation time by 105 minutes. Outcomes for the preliminary analysis included all-cause mortality, cerebrovascular accident (CVA), myocardial infarction (MI), revascularization, and wound reconstruction at 30 days and at one-year, excluding wound reconstruction for the one-year analysis.

Thirty day and one-year mortality did not increase with the use of BIMA. The rate of all-cause mortality at 30 days was 1.2% for both groups. The rate of CVA, MI, and revascularization at 30 days was also similar between the two groups (1.2% vs 1.0% for BIMA, 1.5% vs 1.4% for BIMA, and 0.4% vs 0.7% for BIMA, respectively). BIMA was associated with a slight increase in the risk of sternal wound reconstruction compared with SIMA (0.6% vs 1.9% for BIMA amounting to a difference of 1.3%). The rate of CVA, MI, and revascularization at one-year were similar for SIMA versus BIMA (1.8% vs 1.5%, 2.0% for both, and 1.3% vs 1.8%, respectively). The rate of all-cause mortality for BIMA was 2.5% compared with 2.3% for SIMA.

Preliminary results from ART are promising with regards to the safety and feasibility of BIMA compared with SIMA. Based on these preliminary data, BIMA appears to be safe