News & Views in ...

Interventional Cardiology



News



RESEARCH HIGHLIGHTS







Phase III clinical trial will investigate stem-cell injections as treatment for previously untreatable angina

Researchers at the University of California, Los Angeles (UCLA; CA, USA) have begun an advanced Phase III clinical trial into the use of stem cell therapy in cardiac patient. Specifically, the researchers are investigating whether stem cells may provide new hope for patients suffering from angina and have not responded to US FDA-approved treatment.

This double-blind, multicenter trial involves the use of individuals' own blood-derived stem cells in the hope of restoring the hearts blood supply, which is inadequate in angina. The first individual to participate in the trial had experienced little benefit from other therapies, including a coronary bypass procedure and angioplasty. However, a heart transplant would not be an option as, even after suffering a heart attack, the patient's own heart muscle was functioning well.

"We're hoping to offer patients who have no other options a treatment that will alleviate their severe chest pain and improve their quality of life," comments coprincipal researcher on the trial Ali Nsair (David Geffen School of Medicine, UCLA).

"The first individual to participate in the trial had experienced little benefit from other therapies..."

The patient's own blood is taken and CD34⁺ stem cells are isolated, these express the CD34 protein and are pluripotent. The cells are then purified prior to injection. The stem cell injections are delivered precisely by doctors using a groin artery catheter and are guided by 3D images of the heart. These images are colored and demonstrate the hearts movements, as well as the voltage it generates. The damaged areas produce a smaller amount of energy and motion than those that are undamaged, allowing the targeted stem-cell delivery.



10.2217/ICA.14.1 © 2014 Future Medicine Ltd

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"We are able to tell by the voltage levels and motion which area of the muscle is scarred or abnormal and not getting enough blood and oxygen," reports Jonathan Tobis (Geffen School of Medicine). "We then target the injections to the areas just adjacent to the scarred and abnormal heart muscle to try to restore some of the blood flow."

The researchers are hoping to enroll 444 patients, 222 will receive stem-cell therapy, 111 will receive placebo and 111

will receive current standard care treatment. The researchers further hope that either angiogenesis will be stimulated or new and healthy heart muscle will develop from these pluripotent stem cells, therefore improving blood flow and oxygen provision for the damaged muscle.

Source: University of California, Los Angeles press release: http://newsroom.ucla.edu/portal/ ucla/ucla-injects-stem-cells-into-heart-249258. aspx

Combined use of a balloon guide catheter and stent-retriever device for acute ischemic stroke patients

A study published in *Stroke* has provided evidence for the benefits of using a balloon guide catheter alongside a stent-retriever device in acute ischemic stroke patients. This combined use of devices demonstrates a decrease in procedure time, improved recanalization and overall clinical outcome, according to the present research.

Led by Thanh Nguyen (Boston University School of Medicine, MA, USA) 338 patients were analyzed, 149 of which received the balloon guide catheter, across the 24-center North American Solitaire

New analysis presents the possible benefits of CABG compared with percutaneous coronary intervention

A meta-analysis has identified that coronary artery bypass grafting (CABG) leads to decreased mortality and morbidity rates in patients experiencing multivessel coronary artery disease (CAD) when compared with percutaneous coronary intervention (PCI).

Led by Ilke Sipahi of Acibadem Maslak Hospital (Istanbul, Turkey), the investigation included data from six randomized trials (ARTS, MASSII, SoS, CARDia, SYNTAX multivessel and FREEDOM) completed between 2005 and 2012. A total of 6055 patients with multivessel CAD were included and followed on average for 4.1 years, 3023 received CABG and the remaining 3032 received PCI.

Results of the meta-analysis demonstrated a 27% decreased total mortality in CABG patients compared with PCI. The surgery was also associated with more strokes, but fewer myocardial infarctions and repeat revascularization. This benefit was present regardless of the diabetic status of the patient.

The authors conclude that a more adequately powered study is needed to confirm the benefits of CABG and detect the difference in mortality of CABG compared with medical therapy.

Source: Sipahi I, Akay H, Dagdelen S et al. Coronary artery bypass grafting vs. percutaneous coronary intervention and long-term mortality and morbidity in multivessel disease: metaanalysis of randomized clinical trials of the arterial grafting and stenting era. JAMA Intern. Med. doi:10.1001/jamainternmed.2013.12844 (2013) (Epub ahead of print). Acute Stroke Registry. All individuals involved were treated with a Solitaire FR stent-retriever device (ev3/Covidien, Irvine, CA, USA) for acute ischemic stroke.

Patients, when discharged, experienced a good clinical outcome more often and reported a higher mean NIH Stroke Scale score when they had received treatment with the balloon guide catheter. However, the catheter did not effect the incidence of distal emboli or emboli migration.

After the data were adjusted according to various other factors, the balloon guide catheter still remained a predictor of good clinical outcome (odds ratio: 2.5; 95% CI: 1.2–4.9). However, multivariate analysis of patients who experienced stroke in the posterior circulation did not demonstrate this benefit. The same reduced benefit was also seen in patients who received intravenous tissue plasminogen activator, with discharge mean NIH Stroke Scale scores being lower than nontissue plasminogen activator patients, but good clinical outcome rates still remained high.

These results report the possible benefits of the balloon guide catheter when used in combination with a stent-retriever device; however, this benefit does not apply to all patients and may not always be appropriate.

Source: Nguyen TN, Malisch T, Castonguay AC et al. Balloon guide catheter improves revascularization and clinical outcomes with the Solitaire device: analysis of the North American Solitaire Acute Stroke Registry. Stroke 45(1), 141–145 (2014).

Second-generation drug-eluting stents demonstrated to be as safe as bare-metal stents for STEMI patients

PCI in ST-segment elevation myocardial infarction (STEMI) can be treated with stents. The current study, published in *Circulation: Cardiovascular Interventions*, investigated whether bare-metal stents (BMS) or second-generation drug-eluting stents (DES) provided better outcomes for STEMI patients. The meta-analysis concluded that DES demonstrated the same or better outcomes for patients after 1 year.

Led by Samir Kapadia (Cleveland Clinic, OH, USA), the study authors compared both the long- and short-term efficacy, as well as safety, of second-generation DES with that of BMS, as currently this is an area with limited data. In total, 12,866 randomized patients were included in the research. The network meta-analysis included data from 21 trials that studied first- and second-generation DES and BMS. Specifically, the data included two direct evidence trials (which directly compared second-generation DES with BMS) and 19 indirect evidence trials (four that studied first- and second-generation DES and 15 that investigated BMS and first-generation DES). The majority of patients included were reported to have

a high level of cardiovascular risk factors and to be middle-aged males.

Outcomes assessed included stent thrombosis, target vessel revascularization (TVR) and myocardial infarction (MI), all of which were significantly lower in individuals receiving second-generation DES as apposed to BMS at both 30-day and 1-year follow-up. Mortality rates were demonstrated as not significantly different between the stent groups. Of note, stent thrombosis incidence was demonstrated to be lower as early as 30 days in the second-generation DES patients.

The authors note that the small number of events may have affected the precision of this analysis. The study concludes that second-generation DES usage for PCI in STEMI is not associated with adverse events in comparison with BMS.

Source: Philip F, Agarwal S, Bunte M et al. Stent thrombosis with second-generation drugeluting stents compared with bare-metal stents: network meta-analysis of primary percutaneous coronary intervention trials in ST-segmentelevation myocardial infarction. Circ. Cardiovasc. Interv. doi:10.1161/circinterventions.113.000412 (2013) (Epub ahead of print). "Of note, stent thrombosis incidence was demonstrated to be lower as early as 30 days in the second-generation drug-eluting stent patients."

Anemia negatively affects patient outcomes after transcatheter aortic valve implantation

investigated preoperative anemia in

1696 TAVI patients. The aortic stenosis

patients underwent TAVI between Novem-

ber 2005 and March 2013. The patients

received one of three types of valves, the

SAPIEN or SAPIEN XT (Edwards Life-

sciences, CA, USA), the CoreValve® Sys-

tem (Medtronic, MN, USA), or the Direct

Flow Valve (Direct Flow Medical, CA,

USA). Preoperative anemia was defined

using the WHO criteria, stating anemia

as hemoglobin <13.0 g/dl in men and

<12.0 g/dl in women.

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Transcatheter aortic valve implantation (TAVI) patients can present with preoperative anemia; however, there are little data on the prevalence, associated factors and mortality this is associated with. The present study, published in *Circulation: Cardiovascular Interventions*, demonstrated a 57% rate of preoperative anemia and an association with a higher risk of mortality.

In an observational investigation involving ten centers worldwide, Peter de Jaegere (Erasmus University Medical Center, Rotterdam, The Netherlands) and colleagues The investigation identified that 57% (range: 42–67%) of individuals included in the study presented with preoperative anemia. A number of other factors were associated with the patients being more likely to present with anemia, these included lower BMI, older age and gender, with males more frequently experiencing anemia. Furthermore, following a multivariable logistic regression analysis, preoperative anemia was shown not to be associated with 30-day mortality; however, it did demonstrate an association with 1-year mortality (mortality





"Numerous data and trials have investigated the efficacy and safety of Watchmen™ with primarily positive results, particularly in comparison to warfarin therapy." rate: 21% in nonanemic patients; 31% in anemic patients). Individuals with anemia also received blood transfusions during TAVI, twice as often being given \geq 1 transfusion; this was related to overt bleeding only 40% of the time. The necessity for transfusion was associated with 30-day mortality.

The study concludes that anemia was associated with 1-year mortality and prevalent in over 50% of patients undergoing TAVI. They suggest that the consideration of anemia-associated factors and increasingly strict criteria for blood product usage may improve the outcomes for TAVI patients in future.

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Source: Nuis RJ, Sinning J-M, Rodés-Cabau J et al. Prevalence, factors associated with, and prognostic effects of preoperative anemia on short- and long-term mortality in patients undergoing transcatheter aortic valve implantation. Circ. Cardiovasc. Interv. 6(6), 625–634 (2013).

The Watchman[™] device for nonvalvular atrial fibrillation is one step closer to US FDA approval

An FDA advisory panel have provided support for approval of a new occlusion device in patients with nonvalvular atrial fibrillation (A-fib), the WatchmanTM left atrial appendage (LAA) device (Boston Scientific, MA, USA).

The Watchman LAA device consists of a nitinol cage covered with fabric. It is designed to prevent thrombus embolization that may form in the LAA. The FDA's Circulatory System Devices Panel voted based on the reasonable assurance of device effectiveness and safety. The nearly unanimous (13 to one) vote supports that the benefits the device may present outweigh the possible risks.

The device has been awaiting this kind of support for over 4 years, the present recommendation follows long-term follow-up of the PROTECT AF and the confirmatory results of the PREVAIL trial, both associated with Boston Scientific. In 2009, the FDA panel voted seven to five in favor of the device, but still held three primary reservations. They advised the device be only approved for warfarin-eligible patients, also that doctors undergo full training and only perform the Watchman procedures where cardiac surgery backup was present. The panel recommended the original manufacturers of the device (Atritech, MA, USA) conduct a registry study, which led to the Continued Access Protocol registry that demonstrated better safety and procedure times.

Numerous data and trials have investigated the efficacy and safety of Watchmen with primarily positive results, particularly in comparison with warfarin therapy. The next step for this device will be full approval; however, there are still issues, including the recommended patient population, that need to be resolved.

Source: US FDA. Boston Scientific Watchman left atrial appendage closure therapy executive summary: www.fda.gov/ downloads/AdvisoryCommittees/Committees MeetingMaterials/MedicalDevices/Medical DevicesAdvisoryCommittee/Circulatory SystemDevicesPanel/UCM377356.pdf

- All stories written by Elizabeth Webb

About the News and Views

The News and Views highlights some of the most important events and research in the field of interventional cardiology. If you have newsworthy information, please contact: Michael Dowdall, Managing Commissioning Editor, *Interventional Cardiology*, Future Medicine Ltd, Unitec House, London, N3 1QB, UK; m.dowdall@futuremedicine.com