News from the 2008 Congress of the European Society of Cardiology

Highlights of the European Society of Cardiology meeting held in Munich, Germany, August 30th – September 3rd 2008 showed further benefit for fish oils, this time in heart failure and the first outcome study with the new sinus node inhibitor, ivabradine. There were more equivocal findings for drug-eluting stents, however, and also for statins in heart failure and aortic stenosis.

GISSI-HF shows benefit for PUFA in heart failure

Two new studies from the Italian GISSI group show that n-3 polyunsaturated fatty acids (PUFA) supplementation improves morbidity and mortality in those with symptomatic heart failure, but statins don't have any benefit in the same type of patients.

The results were presented during a hotline session at the Congress and published simultaneously in *The Lancet* (*Lancet* 2008; DOI:10.1016/S0140-6736[08]61239-8, and *Lancet* 2008;DOI:10.1016/S0140-6736[08]61240-4).

Long-term administration of PUFA reduced all-cause mortality by 9%, which the investigators say was a modest effect, and they also cut admission to hospital for cardiovascular reasons. But there was no effect on these same end points with 10 mg of rosuvastatin.

Chair of the GISSI-HF steering committee, Dr Luigi Tavazzi (Fondazione IRCCS Policlinico San Matteo, Pavia, Italy), said PUFA are a safe, effective, simple, and cheap option for patients with chronic heart failure. In an editorial accompanying the published studies (*Lancet* 2008;DOI:10.1016/S0140-6736[08]61241-6), Dr Gregg Fonarow (University of California, Los Angeles, USA) agreed saying: "PUFA should join the short list of evidence-based life-prolonging therapies for heart failure".

GISSI-HF and PUFA

One part of the double-blind, placebo-controlled GISSI-HF (Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico Heart Failure) project investigated the effects of PUFA in patients with New York Heart Association (NYHA) class 2-4 heart failure and randomised them to treatment with n-3 PUFA 1 g daily (n=3,494) or placebo (n=3,481).

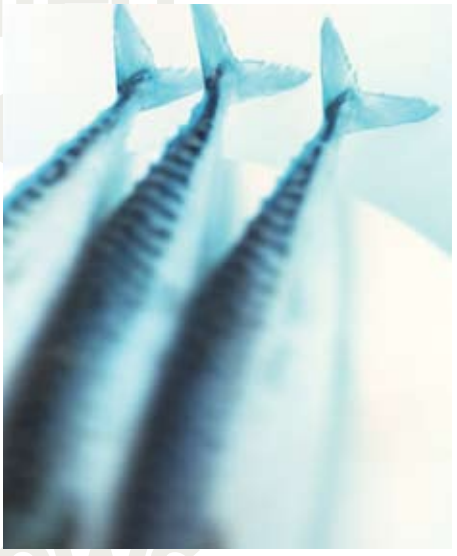
Patients were followed for nearly four years, with the co-primary end points being death, and death or admission to hospital for cardiovascular reasons.

Treatment with PUFA reduced the risk of mortality by 9% and mortality and admission to the hospital for cardiovascular causes by 8%. The absolute risk reduction was small, however. There was no difference in discontinuations and adverse reactions between the PUFA and placebo arms.

Speaking to reporters, Dr Tavazzi said although the exact reasons are unknown, PUFA could possibly exert favourable effects on inflammatory processes. Dr Michel Komajda (Université Pierre et Marie Curie, Paris, France), who was the discussant for the study said there "is still a bit of a mystery" regarding the mechanism of action. Also, few patients with preserved ejection fractions were included, so further analysis will be needed to determine whether the benefit extends to them, he noted.

GISSI-HF and statin therapy

In a separate, nested study presented by Dr Gianni Tognoni (Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy), 2,285 heart failure patients were randomised to rosuvastatin 10 mg daily, while 2,289 were randomised to placebo. There was no significant difference between arms in either of the same two co-primary end points.



Dr Tognoni said that statins should not be prescribed to patients with heart failure because their use does not translate into any clinically meaningful benefit. In his editorial, Dr Fonarow says the GISSI-HF results, alongside the CORONA (Controlled Rosuvastatin in Multinational Trial in Heart Failure) study, "establish that, although statin therapy lowers concentrations of LDL cholesterol, is well tolerated, and seems reasonably safe, it does not produce meaningful improvements in survival in patients with chronic heart failure."

Discussant of this study, Professor Philip Poole-Wilson (Imperial College London) said GISSI-HF is an important study in light of the CORONA findings. "What this study has done is extend what we knew from CORONA, a study where more patients had severe heart failure, to those with less severe heart failure," he said. "To that extent, the two trials are really complementary."

CABG treatment of choice in multivessel/left main disease, SYNTAX finds

Drug-eluting stents (DES) are statistically inferior to coronary artery bypass grafting (CABG), at least for the primary composite end point of the much-awaited SYNTAX trial (Synergy Between PCI with Taxus™ and Cardiac Surgery), for which one-year data were presented at the ESC congress.

SYNTAX randomised 1,800 patients from 62 European sites and 23 in the US who had left main disease, with or without additional coronary disease, or three-vessel disease in all three vascular territories to either CABG (n=897) or PCI (n=903) with the Taxus™ DES. The 12-month primary end point of major adverse cardiovascular or cerebrovascular events (MACCE), including all-cause death, cerebrovascular event, myocardial infarction (MI), and repeat revascularisation (PCI and/or CABG) was 17.8% for the PCI group and 12.1% for the CABG group (p= 0.0015). This was largely driven by the higher rate of revascularisation in the PCI group.

The combined rate of 'hard' end points, however – death, MI, and stroke – were no different between the two treatment groups, and the secondary end point findings were mixed – with a lower rate of stroke among percutaneous coronary intervention (PCI) patients but a higher risk of revascularisation than CABG patients – leading the two main presenters to come to somewhat different conclusions regarding the take-home message of this trial.

The interventional co-primary investigator, Dr Patrick W Serruys (Erasmus University Medical Center, Rotterdam, the Netherlands), told reporters that people "shouldn't leave the room thinking that PCI [with DES] is inferior" just because it did not pass the test for non-inferiority". "It's basically up to the patient to assess the different risks," he said.

But the surgical investigator, Dr Friedrich W Mohr (University of Leipzig, Germany), noted that almost a third of patients considered for randomisation in SYNTAX were deemed ineligible for PCI, primarily due to complex disease or anatomy. So the reality remains that even in the DES era, one-third of patients should not be considered for a percutaneous approach.

He emphasised, more vigorously than Dr Serruys, that the results are "quite clear". "We did not meet the non-inferiority test, so that says that CABG is the treatment of choice – that's clear from those data. And I didn't expect to see that at one year. The advantages of CABG surgery very often appear in the years thereafter, and this needs to be taken into account," he commented.

Dr Serruys conceded that, "technically speaking," the test for non-inferiority was not met. But he emphasised that, until recently, tackling left main disease was "taboo" for interventionalists, and the vast majority of triple-vessel-disease cases were sent directly to surgery.

"I think this will now change. Based on the results, you will see more PCI for main-stem and three-vessel disease, although in which proportion it is difficult to say… You have to realise that we never touched main-stem and three-vessel disease before, and now we have something that shows the same safety profile for PCI and CABG in these cases."

SYNTAX registries

SYNTAX had an 'all-comers' design – patients were randomised if both the interventionalist and surgeon agreed that the patient was eligible for either approach; if one of these strategies was not appropriate, the patient was instead enrolled into one of two 'nested' registries: 1,077 into a CABG registry and 198 into a PCI registry.

In the CABG registry, patients did extremely well, with lower rates of death, MI, revascularisation, and the composite primary end point, than those seen among CABG-treated patients in the randomised trial, despite having some of the most complex lesion anatomy in SYNTAX. By contrast, patients in the PCI registry did considerably worse than their PCI counterparts in the randomised study.

"In patients who are not eligible for PCI, CABG is an excellent option," Dr Mohr concluded. But by contrast, in patients not eligible for CABG, Dr Mohr described PCI as a purely "viable option".

CARDIA: stents versus CABG in diabetes

Results from the CARDIA (Coronary Artery Revascularization in Diabetes) trial show that percutaneous coronary intervention (PCI) may now be considered a reasonable strategy in patients with diabetes with multivessel disease, said Dr Akhil Kapur (London Chest Hospital) who presented the data at the congress.

Like SYNTAX, the CARDIA trial was designed to demonstrate non-inferiority of PCI to coronary artery bypass grafting (CABG) but was confined to patients with diabetes with multivessel disease. Unlike SYNTAX, CARDIA fell short of its planned recruitment, enrolling only 510 patients out of the intended 600, meaning that the non-inferiority parameters set for the trial were not reached due to insufficient power. However, among the 96% to 98% of patients whose events were adjudicated at 12 months, Dr Kapur said there were no differences between PCI and CABG for the primary composite end point of death, stroke and myocardial infarction (MI).

As in SYNTAX, repeat revascularisation procedures were significantly higher among the PCI-treated patients, while strokes were higher among CABG-treated patients, although this difference was not significant. One-year survival rates for the two strategies were almost the same, at 97%.

In a subgroup analysis considering only drug-eluting stents (DES) *vs.* CABG (DES made up 71% of the stents in the PCI arm, the remainder being bare-metal stents), event rates were similar to those of the intention-to-treat analysis, although in this subset, the difference in stroke rates reached significance.

Discussant for the trial Dr Valentin Fuster (Mount Sinai Medical Center, New York, USA), stressed that the trial was underpowered to demonstrate non-inferiority. "In fact, the results are inconclusive," he stated. "I'm not sure we can say PCI in these patients is reasonable; I think the decision clearly needs to be individualised."

BEAUTIFUL results in coronary artery disease

Ivabradine appears to safely lower heart rate, according to the results of the BEAUTIFUL study reported at the meeting, but this had no effect on the study's primary composite end point: cardiovascular death, admission to hospital for acute myocardial infarction (MI), and admission to hospital for new or worsening heart failure in patients with coronary artery disease and left ventricular dysfunction.

Patients with higher heart rates, however, – ≥70 beats per minute (bpm) – appeared to derive some benefit from the drug, even on top of beta-blocker therapy, the investigators said.

Professor Kim Fox (Royal Brompton Hospital, London) presented the BEAUTIFUL (Morbidity-Mortality Evaluation of the I_f Inhibitor Ivabradine in Patients With Coronary Artery Disease and Left Ventricular Dysfunction) results during the first hotline session of the meeting; they were also published in *The Lancet* (*Lancet* 2008;DOI:10.1016/S0140-6736(08)61170-8). A subgroup analysis, also published in *The Lancet*, showed the link between high heart rate and worse

Heart rate is an important predictor of MI

prognosis (*Lancet* 2008;DOI:10.1016/S0140-6736(08)61171-X).

BEAUTIFUL enrolled 10,917 patients from 781 centres in 33 countries, randomising them to 5 mg ivabradine (with the aim of titrating up to 7.5 mg twice per day) or matched placebo, on top of best medical therapy, including high rates of aspirin, ACE inhibitors, and beta blockers. At a median of 19 months follow-up, ivabradine had reduced heart rate by roughly 6 bpm but had no effect on the primary composite end point.

But among a prespecified subgroup of patients having a heart rate higher than 70 bpm at baseline, ivabradine reduced the secondary end points of admission to hospital for fatal and non-fatal MI by 36% and the need for coronary revascularisation by 30%.

Professor Fox said this study was the first time that "pure" heart rate reduction had been explored and showed that it was a "powerful predictor" of MI.

This would have important implications for how patients with cardiovascular disease are managed, he said.

Apart from some instances of bradycardia, the drug was well-tolerated and, according to Professor Fox, supports the safety of ivabradine as an antianginal agent in this population. Ivabradine is already on the market in Europe for the treatment of symptomatic chronic stable angina.

Stormy SEAS: questions over cancer risk with ezetimibe

Much awaited data from the SEAS (Simvastatin and Ezetimibe in Aortic Stenosis) trial were presented at the meeting, and all eyes were on the cancer risks observed with the cholesterol-lowering combination of simvastatin and ezetimibe in this patient population, who had mild to moderate asymptomatic aortic stenosis.

The study also showed that the product was no better than placebo in reducing the primary composite end point of aortic valve and cardiovascular events, something that was first reported earlier this summer. Full results have now been published in the *New England Journal of Medicine*, to coincide with the ESC presentation (*N Engl J Med* 2008;DOI:10.1056/NEJMoa0804602).

SEAS was a randomised, double-blind, clinical trial involving 1,873 patients with aortic stenosis who were treated with 40 mg of simvastatin and 10 mg of ezetimibe or placebo daily. But despite reducing low-density lipoprotein cholesterol levels by 61%, treatment with ezetimibe/simvastatin failed to reduce the risk of the primary end point.

Among those treated with the ezetimibe/simvastatin combination in SEAS, there were significantly more cases of fatal or non-fatal cancer (4.1% *vs.* 2.5%, and 11.1% *vs.* 7.5%, respectively) compared with those treated with placebo. The new cancers, however, were not specific to one site, and a separate independent analysis of ongoing ezetimibe/simvastatin studies – IMPROVE-IT and SHARP – by Sir Richard Peto (Clinical Trials Service Unit, Oxford) and colleagues, also published in the *New England Journal of Medicine*, revealed no increased risk (*N Engl J Med* 2008;DOI:10.1056/NEJMsa0806603). The cancer association, concluded the SEAS investigators, as well as Peto *et al.*, is likely the play of chance rather than a real finding.

"I'm not aware of any data that would support [the hypothesis] that ezetimibe causes fatal cancer within three years after the onset of treatment," SEAS steering committee chair Dr Terje Pedersen (Ulleval University Hospital, Oslo, Norway) told reporters.

But the authors of an editorial accompanying the two papers in the *New England Journal of Medicine* (*N Engl J Med* 2008;DOI:10.1056/NEJMe08072003), say there is uncertainty about the safety and efficacy of the simvastatin and ezetimibe combination.

"Whether the increased risk is due solely to the play of chance is uncertain. Ezetimibe interferes with the gastrointestinal absorption not only of cholesterol but also of other molecular entities that could conceivably affect the growth of cancer cells. The fact that all three trials showed an increase in cancer mortality with ezetimibe should not be assumed to be a chance finding until further data are in."

The analyses by Peto *et al*. have been submitted to the US Food and Drug Administration (FDA) for review. Last month, the agency issued a statement about its investigation but stated that patients should not stop taking simvastatin/ezetimibe combination or any other cholesterol-lowering drug; a full safety report is expected sometime in 2009.

Nine-month data on first biodegradable drug-eluting stent

A new biodegradable drug-eluting stent performed just as well as a conventional sirolimus-eluting stent in the LEADERS (Limus Eluted from a Durable versus Erodable Stent Coating) trial, reported at the ESC by Dr Stephan Windecker (University Hospital, Bern, Switzerland) and also published in *The Lancet* (*Lancet* 2008;DOI:10.1016/S0140-6736[08]61244-1).

LEADERS was conducted in 10 European centres and enrolled 1,707 patients with chronic stable coronary artery disease or acute coronary syndromes to treatment with the biolimus-eluting or the sirolimus-eluting stent. There was no limitation on the number of treated lesions, vessels, or lesion length.

The primary end point – a composite of cardiac death, myocardial infarction (MI), or clinically indicated target vessel revascularisation (TVR) – occurred in 9.2% of patients treated with the biolimus stent and 10.5% of patients treated with the sirolimus-eluting stent, meeting the statistical definition of non-inferiority.

The trial was not powered to address individual components of safety and efficacy. The overall findings were consistent across all subgroups, including those with diabetes and multivessel and small-vessel disease, and in off-label use. In patients with ST-segment-elevation MI (STEMI), however, the primary end point occurred significantly less frequently in patients treated with the biolimus stent.

Investigators also reported data on stent-thrombosis rates. At 30 days, definite or probable stent thrombosis occurred in 2.1% of patients treated with the biolimus stent and in 1.9% of patients treated with sirolimus-eluting stent, a non-significant difference. At nine months, 2.6% and 2.2% in the biolimus- and sirolimus-treatment arms, respectively, had a definite or probable stent thrombosis, also a non-significant difference.

Dr Windecker said the results of the head-to-head could be generalised outside the clinical-trial setting, as the study took on all-comers, including those with multivessel disease and those who had previously undergone revascularisation.

He explained that the new biolimus-eluting stent uses a polymer that degrades into carbon dioxide and water after six months. It leaves behind only the metal mesh, thereafter resembling a bare metal stent. The rationale for the biodegradable polymer is to reduce the risk of late stent thrombosis.

Dr Laura Mauri (Harvard Medical School, Boston, USA), the study discussant, said the hypothesis that the biolimus stent offers long-term safety over the older stents is not yet proven and needed a longer follow-up of over five years to fully prove the hypothesis. Dual antiplatelet therapy should still be given until the safety and efficacy is proven, she said.

ATHENA study shows reduction in stroke in atrial fibrillation

A post hoc analysis of the ATHENA trial, presented at the ESC meeting, found that the antiarrhythmic agent, dronedarone – viewed as a possible alternative to amiodarone – was associated with a 34% (p=0.027) drop in adjusted risk of stroke compared with placebo over a follow-up averaging 21 months in patients with atrial fibrillation/atrial flutter.

Dr Stuart J Connolly (McMaster University, Hamilton, Canada), who presented the findings, said: "No previous antiarrhythmic therapy has been shown to reduce stroke in this way." The reduction occurred in patients who were already adequately treated by standard therapy including antithrombotics, and the effect was consistent in higher-risk patients with different risk factors, he noted.

Dronedarone had already shown a significant 24% decline in time to first cardiovascular hospitalisation or any-cause death, which was its primary end point in ATHENA, as well as significant reductions in risk of cardiovascular mortality (29%), cardiovascular hospitalisation (25%), and arrhythmic death (45%). The main ATHENA findings were reported at the Heart Rhythm Society 2008 Scientific Sessions in May.

ATHENA is one of the largest antiarrhythmic drug trials ever conducted, with 4,628 randomised patients, and dronedarone has so far shown a fairly benign safety profile, putting it in marked contrast to amiodarone. There are still some issues with the new drug, which is under review by regulators in both the US and Europe.

AF recurrence rates for patients taking dronedarone were only modestly better than those for placebo in the EURIDIS and ADONIS trials, and seem slightly poorer than what amiodarone can achieve. There is at least one ongoing trial comparing the two drugs, however DIONYSUS, which may help provide answers. Another potential problem is a possible adverse effect in patients with AF and heart failure, which are frequently seen together. The ANDROMEDA trial was stopped early in 2003 due to an apparent mortality increase associated with dronedarone in the trial's 'high-risk' patients with systolic heart failure.

The discussant at ESC, Dr Karl-Heinz Kuck (Asklepios Clinic St Georg, Hamburg, Germany) reviewed these issues and some other remaining reservations about dronedarone and ATHENA.

The trial enrolled few patients with heart failure and primarily patients with paroxysmal atrial fibrillation, he said, pointing to the need for studies in broader patient groups. Also, the long-term safety of dronedarone needs exploring, given ATHENA's finding of a somewhat higher incidence of elevated creatinine associated with the drug in a few cases, he noted.

"When we have all these questions answered, we may know what place there may be for dronedarone for maintaining sinus rhythm and to prevent stroke and for other indications in patients with atrial fibrillation," he said adding that: "My personal view is that the stroke reduction by more than 30% is one of the most important findings of this trial".

Mixed results for TRANSCEND study in ACE-intolerant patients

The angiotensin-receptor blocker (ARB) telmisartan has fared no better than placebo in the TRANSCEND study (Telmisartan Randomized Assessment Study in ACE-Intolerant Subjects With Cardiovascular Disease) in patients at high risk of cardiovascular disease unable to tolerate ACE inhibitors.

But the trial did show a modest benefit of the drug on the prespecified composite secondary outcome and demonstrated that it was safe to use an ARB in patients who had previously had severe reactions to ACE inhibitors.

The large TRANSCEND study was carried out in 630 centres in 40 countries on 5,926 patients with cardiovascular disease or high-risk diabetes without heart failure who were intolerant to ACE inhibitors. They were randomised to telmisartan 80 mg per day (n=2,954) or placebo (n=2,972) in addition to other usual therapies.

After 56 months follow-up, there was no difference in the primary composite end point of cardiovascular death, myocardial infarction (MI), stroke, or admission to hospital for heart-failure events, which occurred in 465 (15.7%) of patients taking telmisartan and 504 (17.0%) of those on placebo (hazard ratio 0.92; p=0.216).

There was a difference in the prespecified composite secondary outcome of cardiovascular death, MI, and stroke, however, with 384 such events in the telmisartan group (13.0%) *vs.* 440 (14.8%) in those on placebo (hazard ratio 0.87; p=0.048).

ARBs, which are viewed as better tolerated than ACE inhibitors, have shown benefit in heart failure, moderate hypertension and left ventricular hypertrophy, but this was the first study to look at their use in a broader, high-risk population.

Dr Koon K Teo (McMaster University, Hamilton, Canada) who reported the findings of TRANSCEND at the congress with simultaneous publication of the results in *The Lancet* (*Lancet* 2008; DOI:10.1016/SO140-6736[08]61242-8) said that the study showed that telmisartan was very well tolerated in a large group of patients with a lower rate of discontinuation than placebo, which he called "remarkable". He stressed that there was a " quite strong" trend toward a reduction in MI and stroke among those taking telmisartan, "but the neutral effect on heart-failure events was surprising."

TRANSCEND and its much larger sister study ONTARGET were designed as the biggest comparisons to date of ARB and ACE-inhibitor therapy in high-risk patients with controlled blood pressure, and the results were expected to contribute significantly to the future treatment of cardiovascular disease. ONTARGET, reported earlier this year, showed that telmisartan was non-inferior to ramipril in terms of blood-pressure-independent cardioprotection.

Discussant of TRANSCEND Dr Karl Swedberg (Sahlgrenska University Hospital, Gothenburg, Sweden) said: "The preventive effects of telmisartan are at best modest," and he wondered, "how telmisartan can be non-inferior to ramipril (based on ONTARGET) but barely better than placebo." The findings, he said, "illustrate the complexity of interpreting different patient populations and trying to come up with a conclusion".

Accompanying the TRANSCEND paper in *The Lancet* is a Comment by Drs Toni L Ripley and Donald Harrison (University of Oklahoma College of Pharmacy, Oklahoma City, USA) (*Lancet* 2008;DOI:10.1016/SO140-6736(08)61243-X).

They say the failure of telmisartan to reach the primary end point in this study is "unexpected" and that there are several possible reasons for this. First, it was too ambitiously powered and second, there may be heterogeneity in the ARB class. ACE inhibitors "should remain the preferred renin-active agent to prevent vascular events in patients with or at high risk for cardiovascular disease," they conclude.

The study results should also not obscure important safety information, they stress. In TRANSCEND, 377 patients had previously had severe reactions to ACE inhibitors that would, "until these data, preclude use of an ARB".

TRITON-TIMI 38: promising results for prasugrel in ACS

A subgroup analysis of the TRITON-TIMI 38 trial released at the meeting shows that patients with diabetes who were diagnosed with acute coronary syndrome (ACS) were 40% less likely to suffer a myocardial infarction (MI) if they were treated with prasugrel rather than clopidogrel, (8.2% *vs.* 13.2%, respectively, p<0.001).

The analysis showed that the combined rate of cardiovascular death, non-fatal MI and non-fatal stroke was also reduced by 30% in diabetes patients treated with prasugrel compared to those treated with clopidogrel (12.2% *vs.* 17.0%, respectively, p<0.001).

Rates of major bleeding events were similar for prasugrel and clopidogrel (2.5% *vs.* 2.6%, respectively) among patients with diabetes, regardless of diabetes therapies (insulin versus no insulin).

The main TRITON-TIMI 38 clinical trial compared prasugrel with clopidogrel in patients with ACS undergoing percutaneous coronary intervention (PCI). In the primary analysis of the trial, prasugrel reduced the risk of the composite end point of cardiovascular death, MI, or stroke by 19%, with an increased risk of major bleeding compared with clopidogrel (2.4% *vs.* 1.8%).

In addition to the results reported above, the reduction of cardiovascular events was consistent across the subgroup of diabetes regardless of diabetic therapies (insulin versus no insulin). The study showed a significant relative risk reduction in the primary end point of cardiovascular death, non-fatal MI and non-fatal stroke with prasugrel of 37% for insulin treated and 26% for non-insulin treated patients with diabetes (p=0.001). There was also a significantly lower rate of stent thrombosis among diabetes patients treated with prasugrel resulting in a 48% relative risk reduction in stent thrombosis compared with clopidogrel (3.6% *vs.* 2.0%, p=0.007).

CONGRESS REPORT

Perioperative statin cuts CV deaths in vascular surgery patients

Use of extended-release fluvastatin perioperatively in patients undergoing vascular surgery who were not already taking a statin led to a nearly 50% reduction in myocardial ischemia and a similar reduction in cardiovascular death/non-fatal myocardial infarction (MI) in the DECREASE III (Dutch Echographic Cardiac Risk Evaluation Applying Stress Echo III) trial.

The results were presented at the meeting by Professor Don Poldermans (Erasmus Medical Center, Rotterdam, The Netherlands). In the study, almost 500 statin-naive patients scheduled to undergo vascular surgery were randomised to a sustained-release formulation of fluvastatin (n=250) 80 mg per day or placebo (n=247) an average of 37 days prior to surgery. The statin was continued for at least the first 30 days after surgery.

The primary end point was incidence of myocardial ischaemia, as assessed by a combination of continuous ECG monitoring in the first 72 hours and then intermittent troponin-T measurements and further ECGs until the end of follow-up, on day 30.

There was a clear reduction in the primary end point among those taking fluvastatin – 27 patients in the statin group (10.9%) had myocardial ischaemia compared with 47 (18.9%) in the placebo group (OR 0.53; p=0.016). The number needed to treat (NNT) to prevent one patient experiencing myocardial ischaemia was 12.5.

There were similar findings for the combined secondary end point of cardiac death or non-fatal myocardial infarction (MI), which was significantly reduced among those taking the statin. Twelve (4.8%) of those taking fluvastatin met this end point compared with 25 (10.1%) of those on placebo (OR 0.48; p=0.039).

Professor Poldermans said he thought it was time to change the guidelines as a result of this large study, which comes on the heels of a smaller Brazilian one showing similar findings, as well as some retrospective studies. Doctors should know that if patients have peripheral arterial disease (PAD) and are undergoing vascular surgery – though they might not have an increased cholesterol level – they still benefit from statins, he noted.

He said around 950,000 vascular surgeries are performed every year, with a 2% rate of cardiovascular death, much of which is due to perioperative MI. He also stressed the safety aspect: "There was no evidence of increased liver dysfunction or myopathy in those taking fluvastatin in DECREASE III," he said.

In brief

Editorial board appointment

We are delighted to welcome Dr Anthony Wierzbicki (right), Senior Lecturer in Chemical Pathology, St Thomas' Hospital, London to the editorial board. Tony is internationally renowned in the field of lipid medicine and plays a very active role with H.E.A.R.T UK. We look forward to his lively and informative contributions to the *BJC*.

EMEA approval for ranolazine and bosentan

Ranolazine (CV Therapeutics) has received marketing authorisation from the European Medicines Agency (EMEA) for the treatment of patients with chronic angina in all 27 European Union (EU) member states. Ranolazine is approved for use in Europe as add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled or intolerant to first-line antianginal therapies. Ranolazine is approved for use in 375 mg, 500 mg and 750 mg doses, administered twice daily.

Bosentan has been approved for the treatment of patients with mildly symptomatic pulmonary arterial hypertension (PAH WHO functional class FC II). This follows its approval in the European Union in 2002 for PAH patients with WHO FC III.

NICE guidance on FH

The National Institute for Health and Clinical Excellence (NICE) has issued new guidance on the identification and management of familial hypercholesterolaemia (FH). The full guidance can be found on www.nice.org.uk.

Key recommendations include:

- cardiovascular risk calculators should not be used to assess risk and inform future management in people who fit the FH criteria
- individuals with suspected FH should be referred to a specialist for confirmation of diagnosis and initiation of cascade testing (assessing all first and second degree relatives for the condition)
- a blood cholesterol test for children of individuals with FH by the age of 10
- a nationwide family based follow-up system to enable comprehensive identification of affected individuals
- statins should be offered as first-line treatment and individuals with FH should be regularly monitored, at least annually. Adults with the condition should be treated with high-intensity statins to reduce low-density lipoprotein cholesterol levels by 50%.

Michael Livingston, Director of H.E.A.R.T UK, whilst welcoming the guidance, pointed out that many people with the condition go undetected. About one person in every 500 in the UK has FH but 20% are undiagnosed. "The next step for us will be to ensure this guidance is implemented on the ground," he said.