Antidepressant therapy in heart failure patients called into question

Depression in chronic heart failure improves with optimised heart failure management, irrespective of antidepressant therapy, and may be a complication of the condition, delegates heard in a Late Breaking Trial session this morning.

Presenting an analysis of the MOOD-HF study, Christiane Angermann, from University Hospital Wuerzburg, Germany, showed that Montgomery–Åsberg Depression Rating Scale (MADRS) scores improved significantly after 12 weeks both in patients treated with escitalopram and those who received placebo.

Noting that the patients also experienced improvements in heart failure severity and cardiac function, she told Heart Failure Congress News ahead of her presentation: “That depression got better in this early phase is maybe not only a placebo effect but, at least in part, also an effect of improvement in heart failure.”

“It raises the question whether comorbid depression in heart failure is really a disease entity in itself or whether this should to some extent be considered a complication of heart failure itself, and that improving heart failure maybe a means to also improve comorbid depression.”

For the study, chronic heart failure patients were randomised to escitalopram once daily (n=185) or placebo (n=187), which was up-titrated over 12 weeks, alongside concomitant optimisation of chronic heart failure therapy.

The patients were then followed for up to 24 months, with the primary endpoint time to death or unplanned hospitalisation. Professor Angermann emphasised that MOOD-HF is unique among trials evaluating the effects of an antidepressant in heart failure patients, as no other comparable study has had such a long follow-up.

The primary endpoint occurred in 63% of escitalopram patients and in 64% of placebo patients, at a hazard ratio (HR) of 0.99 (p=0.92). At 12 weeks, MADRS scores decreased from 20.2±8.5 to 12.5±8.1 in the escitalopram group, and from 21.4±8.5 to 12.5±7.6 in placebo patients (p<0.001 for both).

Post-hoc subgroup analysis was based on binary analysis of the heart failure risk factors median age, New York Heart Association class, left ventricular end-diastolic diameter, N-terminal pro brain natriuretic peptide and heart rate.

This indicated that escitalopram had heterogeneous effects on heart failure parameters. However, depression symptoms improved significantly at 12 weeks regardless of subgroup, and there was no interaction between escitalopram treatment and improvement in depression (p=0.82).

Commenting on the lack of effect of antidepressant therapy on both depression symptoms and the clinical endpoints, Professor Angermann stated: “One would, against this background, not recommend treating these patients with an antidepressant. That’s the central message of the trial.”

The findings also raise questions both in terms of the pathophysiology of depression in chronic heart failure, and the way antidepressants are marketed by pharmaceutical companies.

“When an antidepressant is tested for the market, it is usually evaluated in physically healthy depressed human beings,” Professor Angermann said. “There are no marketing studies in physically ill patients like heart failure or myocardial infarction patients.”

She continued: “So the whole marketing strategy for this type of drug needs to be reconsidered when one now observes that a condition that is depression according to the gold standard instrument, which is the structured clinical interview performed by a psychiatrist, which we applied, diagnoses a depression which does not respond to the antidepressant.”

In conclusion, Professor Angermann said: “It shows that comparable symptoms may perhaps have a heterogeneous pathophysiology; our data suggest that pathophysiology and treatment requirements may differ in someone with cormorbid depression from someone who is physically healthy but is depressed.”
Towards Effective Heart Failure Treatment - A Tale of Two Cities

This afternoon, in the first Heart Failure Association (HFA) Philip Poole-Wilson Lecture, Henry Dargie will explore the influence the Glasgow/London axis had on the development of effective heart failure care in the UK. The lecture is the keynote speech opening the Young Investigator Clinical Award session (14:15-15:45, Agora).

The lecture honours the memory of Philip Poole Wilson (1943-2009), a great advocate for research in heart failure, who served as president of the ESC from 1994 to 1996. Among many heart failure contributions, Poole-Wilson introduced the six-minute walk test for assessing heart failure, undertook basic science research in heart muscle contraction, played a key role in development of heart failure guidelines and was involved in many clinical trials including COMET.

“Philip was a good friend and colleague whom I first met in the mid-1970s at the London Blood Pressure Club, an informal group for young researchers studying hypertension,” says Dargie, from the University of Glasgow. “Paradoxically, involvement in heart failure for both of us began with the quest for more effective hypertension treatments. A revolution in new medicines for heart failure started when the benefits of ACE inhibitors alone, followed by their combination with beta blockers, became apparent.”

For many years, heart failure in the UK was dominated by a Glasgow/London axis led by Dargie and Poole-Wilson. Appointed as a consultant cardiologist in Glasgow in 1980, Dargie built up a concentration of heart failure expertise with interests in epidemiology, clinical trials, imaging and clinical management. It is noteworthy that many of the most prominent heart failure experts in the UK, including John Cleland, John McMurray, Theresa McDonagh and Andrew Clark, began as research fellows in his unit at the Western Infirmary.

Poole-Wilson, Dargie and others became aware that heart failure in the UK was being left behind by the advances in other areas of cardiology despite it being a major public health issue. This led to the founding of the British Society for Heart Failure (BSH) in 1998, with Poole-Wilson as the first chairperson. As BSH chairperson in 2003, Dargie was instrumental in setting up and running the National Heart Failure Audit (NHFA) in the UK. Now at the National Institute for Cardiac Outcomes Research (NICOR) in London, this work has been associated with a continuing pattern of improvement in adherence to guidelines and survival in patients admitted to hospital with acute heart failure.

Dargie has also led a number of large clinical trials including CIBIS II (with the β blocker bisoprolol in heart failure) and CAPRICORN (with carvedilol in patients with left ventricular dysfunction or heart failure following MI) I. “These trials helped the use of β blockers to become guideline recommended practice in heart failure,” he says. Beta blockers were invented by James Black who also invented cimetidine, the first effective medicine for gastric and duodenal ulcers for which he received the Nobel Prize. “A major highlight of my career was when Professor Black visited us to discuss the use in heart failure of the highly selective β 2 adrenoceptor antagonist he had invented while with ICI,” says Dargie.

Dargie’s tip to young colleagues embarking on careers in heart failure is to follow what they are interested in. “These days collaborative research is the name of the game, and the best way to find such collaborations is through your national association and the HFA,” he says.

Focus sessions: new app allows delegates to vote with smart phones

For the first time at a Heart Failure congress, the HFA Focus sessions are interactive: the audience is invited to vote and ask questions via the official ‘Heart Failure 2015’ congress Mobile App.

First launched at the 2010 Heart Failure meeting in Berlin, the Focus sessions have now become a much anticipated part of the meeting. “Focus sessions undoubtedly represent a major part of the congress educational experience alongside clinical trial updates and guideline sessions. Clinical trial updates tell delegates what’s new, guidelines tell them what to do, while Focus sessions provide valuable insights into how to apply this information to real-world patients,” says Gerasimos Filippatos, the President of the HFA. “Focus sessions are really popular because they provide practical take home messages you can immediately start applying to your everyday clinical practice.” Everyone whatever their level of seniority, he adds, has something to learn from Focus sessions, whether HF experts, family doctors, nurses or trainees. Experts can voice their own opinions while trainees can consider the different points of view of experts and come to their own decisions.

“For all concerned the process helps to encourage critical thinking,” says Filippatos.

In each of the four sessions three international experts will present short case studies from their own clinical experience and then pose questions to the audience. The distinguished faculty includes Sean Collins from Nashville, Raphael Rosenhek from Vienna, Theresa McDonagh from London, and Cecilia Linde from Stockholm. A major part of the learning experience is for delegates to compare their own answers with expert opinion. A panel of expert discussants will be on hand to debate any controversial issues that arise, with further possibilities for informal open floor discussions around treatment options and prognosis. The case studies are always linked back to the latest ESC Guidelines on the diagnosis and treatment of HF.

“The presentations often provide helicopter views that can identify where there may be gaps in the guidelines we have not appreciated and will address,” says Filippatos.

Introducing the interactive voting via the Mobile App – thus providing the opportunity to use the familiar interface of your own smart phones, the HFA hopes, will bring a new dynamic to these popular sessions. Delegates will additionally be able to use their phones to pose questions directly to the moderators. “We really hope that the new technology will help us to have our best ever audience participation,” says Filippatos, from the University of Athens.

Call to Action!

Pick up your copy of the White Paper – the HFA’s vision on building a common approach across and beyond Europe to raising heart failure awareness amongst targeted audiences
Hyperkalaemia in heart failure patients rapidly normalised with novel drug

A novel drug that selectively binds potassium in the intestine rapidly normalises serum potassium levels in heart failure patients with hyperkalaemia, thus offering the possibility optimal administration of cardioprotective therapies, revealed results presented yesterday.

During yesterday’s Late Breaking Trials session, Stefan Anker, from Goettingen, Germany, showed that the selective cation exchanger sodium zirconium cyclosilicate (ZS-9) normalises serum potassium levels within 48 hours. In addition, the drug maintains potassium levels over 4 weeks.

Hyperkalaemia is a frequent problem in cardiovascular disease patients treated with angiotensin-converting-enzyme (ACE) inhibitors and aldosterone antagonists, particularly those with heart failure.

Speaking to Heart Failure Congress News ahead of his presentation, Dr Anker noted that hyperkalaemia often limits the therapeutic options available for heart failure patients.

“It creates side effect problems, it can cause arrhythmias and basically stops people from using the drugs to the extent they should be used,” he said.

“So we really have a big medical need to take care of this if we want to treat our heart failure patients with drugs that have inherently this hyperkalaemia side effect.”

The data come from a subgroup analysis of the original double-blind, randomised, placebo controlled trial of ZS-9, in which patients were treated with 10 g ZS-9 three time daily with meals for 48 hours. Those achieving normal potassium values were then randomised to 5 g, 10 g or 15 g ZS-9 or placebo for 28 days. The current analysis included 94 heart failure patients with hyperkalaemia.

In the open-label phase, mean potassium levels reduced from 5.6 mmol/l to 4.4 mmol/l, with 99% of patients achieving normal potassium levels by 48 hours. During the randomised phase, potassium levels were maintained at 4.7 mmol/l, 4.4 mmol/l and 4.4 mmol/l in the 5 g, 10 g and 15 mg ZS-9 groups, respectively, compared with 5.1 mmol/l in the placebo group (p<0.01).

In addition, normal potassium levels were maintained in 83%, 89% and 92% of ZS-9 patients, respectively, compared with just 40% of placebo patients. ZS-9 was also well-tolerated, with a similar adverse effect profile to that of placebo.

Discussing the findings, Dr Anker explained: “Compared to placebo, this is a very effective treatment in achieving normal kalaemia. If you continue this treatment for a longer period of time, such as for 4 weeks, you maintain normal potassium values, whereas if you are switched to placebo, your potassium values go up again. He continued: “This basically again limits the use of good cardiovascular medicines like ACE inhibitors, like aldosterone antagonists, that we want to give these patients.”

Following these promising findings, the next step is for the company to obtain regulatory approval in Europe and the USA for using ZS-9 either to reduce high to normal potassium levels or to maintain patients at high risk of developing hyperkalaemia.

In the future, trials are required showing the effect of drug exposure over one or two years, to determine whether patients who are currently on low doses of ACE inhibitors or aldosterone antagonists can be safely uptitrated without worrying about potassium levels.

Dr Anker commented: “There should be, if you like, a study to see whether a higher frequency of guideline-approved doses of ACE inhibitors or aldosterone antagonists can be achieved against the background of these drugs.”
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Educational offer

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Heart Failure is the annual congress of the Heart Failure Association of the ESC

What is the biggest benefit of presenting an abstract at the Heart Failure congress?

For me, a relative greenhorn PhD student, the Heart Failure congress means an opportunity to present my very first results. As I have been accepted for a moderated poster presentation, I have a window of five minutes to present my research. Considering the magnitude of the congress, I hope to reach a great audience and expect critical appraisals of my work.

Furthermore, I hope that the presentation will attract other investigators who are also interested in my research topic (Cardiac Resynchronization Therapy) so that we may exchange thoughts. From there, new ideas and collaborations can arise. We’ll see!

The biggest benefit of presenting my abstract at the Heart Failure congress is to be a part of the scientific world, to gain experience by communicating with colleagues from different countries and to improve my potential as a young doctor and scientist.

There are opportunities to learn the latest trends in the management of patients with heart failure, and then to successfully implement it in my routine practice.

Presentation of my research results at this significant congress gives me confidence and helps me to understand that I’m heading in the right direction.

I am a clinical research fellow at the Royal Brompton Hospital in cardiology; exploring barriers to diagnosis and treatment of sleep disordered breathing (SDB) in cardiovascular disease.

SDB or sleep apnoea is an important disorder, with up to 30-40% of heart failure patients suffering from it (this corresponds to ~320,000 patients in the UK!). A recent British Lung Foundation report suggested that 80% of these patients could be undiagnosed. Therefore, I believe the biggest benefit in presenting my work at the Heart Failure congress is raising the profile of SDB in cardiovascular disease.

Potentially, raising awareness may improve the diagnosis and treatment of these patients; so far we’ve only seen the tip of the iceberg!