AHA 2010 - Forgotten drug Inspra surprises in mild heart failure

Jonathan Gardner

Pfizer’s Inspra fizzled on takeoff, but has a new taper been lit? Trial data presented at the American Heart Association meeting suggests that the anti-hypertensive averts death and hospitalisation in heart failure patients with mild symptoms.

The findings of the Pfizer-sponsored trials are not likely to reverse the fortunes of the onetime blockbuster-in-waiting. However the drug, currently indicated for the more seriously ill congestive heart failure (CHF) patients following a heart attack, could now be used in a much wider population.

The once and future CHF drug

Introduced for CHF in 2003, Inspra belongs to a class of drugs called aldosterone antagonists. The first drug in the class is spironolactone, which has been available since 1959. Their original use was as adjunctive therapy to other medicines for additive diuretic effect, but more recent research has shown that aldosterone antagonism also prevents scarring and fibrosis in an enlarged heart, as well as conserving potassium and magnesium, and thus prevents arrhythmia and sudden death.

Inspra is a more selective aldosterone antagonist and was thought to have fewer side effects than spironolactone. However, Inspra performed so badly following its launch that Pfizer ceased revealing sales figures in 2005, when it generated just $8m.

The world’s largest pharmaceutical company attributed the poor performance to physicians’ failure to adopt aldosterone blockade as the standard of care in heart failure. Despite the disappointing results, the New York group has not given up on the compound it inherited with its purchase of Pharmacia in 2004.

The findings from the Emphasis-HF trial detailed Sunday in Chicago and published simultaneously by the New England Journal of Medicine suggest the drug may have found a new niche in untreated or undertreated mildly ill CHF patients. Indeed, the efficacy was positive enough that investigators ended enrolment early because of overwhelming benefit. Patients were 37% less likely to die or be hospitalised due to heart failure, than those on standard therapy.

Faiez Zannad, the lead investigator and a professor at Nancy University Hospital in France, said that Inspra should be considered for all patients.

“This is an exciting day indeed that we can talk about a newer patient population for this drug, but we still have a lot of work ahead of us,” Mariell Jessup, a professor at the University of Pennsylvania medical school, said of the findings.

Class effect

Others, however, argue that the findings showing Inspra superior to placebo are more indicative of undertreatment of mildly ill CHF patients more generally with aldosterone antagonists. This was the case made in a NEJM editorial by Paul Armstrong, a professor at the University of Alberta medical school, published in conjunction with the Emphasis-HF trial data.

As a decades-old product, spironolactone is a cheaper drug, so the more expensive new drug should be restricted to those who find spironolactone’s side effects “disabling,” Dr Armstrong wrote.

Given that spironolactone and Inspra share hyperkalaemia as a major side effect, it is not necessarily clear that Inspra has a better side effect profile, adds Clyde Yancy, medical director of the Baylor University Heart and Vascular Institute.

“I’m enthusiastic about the expansion in the indicated population but my enthusiasm is tempered until we see
a bit more and understand a bit more about the hyperkalemia,” Dr Yancy said.

Pfizer’s research has answered a key scientific question about Inspra - it does address an unmet medical need in CHF treatment which will hopefully benefit patients. But given generic competition and the fact that even Inspra patents have now expired, it seems unlikely the drug's original developer will benefit from this new knowledge.

Trial ID NCT00232180 (Emphasis-HF)