Evaluate Vantage

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AHA preview – Daiichi blood-thinner data takes the spotlight

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In the wake of long-awaited new US cardiovascular disease guidelines the American Heart Association conference kicks off in Dallas this weekend, and will no doubt feature vigorous debate about these risk-based recommendations, which have already prompted controversy among physicians.

On the therapeutics side the debate will turn to the fourth novel anticoagulant in recent years, Daiichi Sankyo's Lixiana, which will have its pivotal stroke prevention data readout, while the use of cell therapies to regenerate damaged heart and vascular tissue continues to receive attention. With the heralded PCSK9 inhibitor class now destined for long-term outcomes studies the spotlight will shift to other projects in development. And the first human trial of Humacyte's tissue-based vascular graft will show whether the lab-grown acellular grafts can improve blood vessel access in haemodialysis patients.

Late to the party

Lixiana has been on the market in Japan since 2011, and could become the third factor Xa inhibitor and fourth novel anticoagulant to be launched in the US in recent years. In September Daiichi released data from the 8,300-patient venous thromboembolism (VTE) study Hokusai-VTE, in which the factor Xa showed non-inferiority on thromboembolic events and significant superiority in occurrence of major bleeding incidents compared with warfarin (*ESC – Daiichi joins the US-EU blood-thinning race with positive Lixiana data, September 2, 2013*).

In getting positive data in VTE, Daiichi has followed a tried and tested path to major launch. The company is ultimately aiming for approval for stroke prevention in patients with atrial fibrillation, a much bigger prize.

The 20,000-patient Engage-AF-Timi trial pits Lixiana, known generically as edoxaban tosylate, against warfarin over 24 months, with the primary endpoint of stroke and systemic embolic events. It would be considered a huge win if the drug shows superiority over warfarin in both stroke prevention and on bleeding safety endpoints.

With a once-daily dosing interval and strong stroke data, the drug would be viewed as a strong new competitor. But getting to launch is no guarantee of commercial success, either. Despite much clinical promise having been offered by the new generation of anticoagulants when compared to warfarin, Johnson & Johnson and Bayer's factor Xa inhibitor Xarelto is the only one that has truly hit – Bristol-Myers Squibb and Pfizer's Eliquis has struggled (*Vantage Point – As Eliquis limps on Xarelto dominates oral blood thinners, October 9, 2013*).

Elsewhere, with long-term outcomes studies having put off all hope of a launch of PCSK9 antibodies for several years, the discussion surrounding them at AHA will probably centre on their need to show a mortality benefit, rather than reduction in low-density lipoprotein, as a result of the new recommendations (*New US cholesterol guidelines reinforce the importance of outcomes data, November 13, 2013*).

Whither stem cells?

Meanwhile, another much-hyped approach to the intractable area of heart failure will get a special session. Use of bone marrow-derived and mesenchymal stem cells in regenerating the diseased tissue of patients on left-ventricular assist devices (LVADs) awaiting transplants is of particular interest, as is the effect of sitagliptin plus granulocyte colony-stimulating factor in patients with myocardial infarction.

Researchers have been outlining data from trials of cell therapies at AHA for several years, but these appear little closer to the market, and with only one stem cell therapy on the Western markets so far the regulatory path is far from easy.

However, the fact that investigators appear to have homed in on a specific subpopulation – LVAD patients – suggests that they have identified people with a particular medical need.

Humacyte, by contrast, is examining the effects not of cells but of their absence. Haemodialysis often

necessitates the connection of an artery to a vein to speed blood flow during treatments, for which a graft in the arm is used. Synthetic grafts can cause clotting, and harvesting veins from the patient's own body involves a separate procedure, with the attendant risks of infection and other complications.

Humacyte's biological vascular graft is grown from allogeneic cells in a bioreactor and then decellularised, yielding only human extracellular matrix, which will avoid the problems with other materials and prevent an immune response. Results of its first human trial will show whether the product has potential to improve quality of life for the 320,000 patients in the US alone who require regular dialysis.

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