

Dolutegravir sailing toward key regulatory dates



[Jonathan Gardner](#)

In releasing data from the Sailing trial of dolutegravir, GlaxoSmithKline has wrapped up most of the data necessary for regulatory review of what is forecast to be the third-biggest drug launch of 2013. The HIV integrase inhibitor is not expected to match sales of Gilead Sciences' top-seller Stribild, but it will be a useful earner that could help shore up the UK group's eroding franchise.

With superiority to Isentress demonstrated in the trial, dolutegravir should have a good chance at challenging Merck & Co's dominance in the integrase inhibitor class. Approval decisions on both sides of the Atlantic are due in the second half of 2013, meaning that dolutegravir's progress will be closely watched.

Achieving superiority

Sailing compared dolutegravir's effectiveness with Isentress in HIV patients whose virus is resisting antiretroviral therapy but who have not been treated with an integrase inhibitor. Patients either took dolutegravir plus a twice-daily Isentress placebo or Isentress plus a once-daily dolutegravir placebo, both on a background of antiretroviral therapy.

Viiv Healthcare, GSK's HIV joint venture with Pfizer and Shionogi, announced that on once-daily dolutegravir, 79% of patients achieved viral suppression after 24 weeks, which compared favourably against the 70% of patients on Isentress. The finding was driven by superior response in patients taking dolutegravir, the company said – 15% of dolutegravir patients showed no response and just two failed, compared with 24% non-response and 10 failures altogether on Isentress.

Adverse events were judged to be similar, with 2% of dolutegravir patients having withdrawn, compared with 4% of Isentress patients.

Sailing was revealed at the Conference on Retroviruses and Opportunistic Infections, and is one of four pivotal studies to support dolutegravir's registration. Two have been completed: Spring-2 and Single, both in treatment naïve patients, the former in combination with Isentress vs Isentress monotherapy, the latter in combination with antiretroviral therapy vs Atripla monotherapy.

A fourth, Viking, is testing dolutegravir in patients who have shown resistance to Isentress or elvitegravir, the Gilead Sciences integrase inhibitor that is also a part of the four-drug cocktail Stribild. Viiv has disclosed 24-week data on Viking; 48-week data are awaited, as with the Sailing trial.

Return to form

A successful commercial launch of dolutegravir would be a return to form of sorts for Viiv's majority owner, Glaxo – an FDA action date has been set for August 17. Its predecessor company Burroughs-Wellcome had launched the very first HIV drug in the form of Retrovir (AZT), and as recently as 2005 the UK group had the best-selling drug in the space in the form of the blockbuster NRTI Combivir, with helpful assists from fellow NRTI's Trizivir, Epivir and Ziagen.

Glaxo has not launched a new HIV drug since Epzicom, a combination of Ziagen and Epvir, in 2004. This is now Viiv's biggest seller, forecast to sell \$1.18bn this year, declining to \$746m in 2018 following generic entry in 2016, according to *EvaluatePharma* data. In forming Viiv with Glaxo, Pfizer brought along Selzentry, launched in 2007.

Thus in dolutegravir Glaxo is reasserting itself in the relatively new integrase inhibitor class, six years after Merck launched Isentress. Unlike Gilead, which has chosen first to put elvitegravir into combinations like Stribild, Viiv has decided to premiere its integrase inhibitor as a single pill to be used on top of a separate retroviral backbone.

As a monotherapy, dolutegravir is forecast to reach \$1.32bn in sales in 2018. A single-tablet regimen with Ziagen and Epivir, known variously as dolutegravir-Trii or '572-Trii, is in phase III.

When Glaxo formed Viiv with Pfizer, a partnership that has since been enhanced with the addition of Shionogi, the two companies were acknowledging their relative weakness in a space where much of the innovation was

emerging from Gilead ([Glaxo and Pfizer to join forces on HIV, April 16, 2009](#)). Success with dolutegravir would be a good first step back toward relevance.

Study	Trial ID
Sailing	NCT01231516

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