Evaluate Vantage

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Gilead and Glaxo’s HIV battle intensifies

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The first phase II data with Gilead’s HIV integrase inhibitor bictegravir have set up a showdown with Glaxosmithkline/Viiv Healthcare’s marketed product dolutegravir. But Glaxo is already one step ahead with data from a two-drug combo that could reduce the side-effect burden for HIV patients.

Glaxo believes that this doublet could “reshape the whole game”, the group's chief executive, Andrew Witty, said on its fourth-quarter earnings call. HIV has been one of the group’s main drivers in recent quarters as it has taken market share from Gilead, which is becoming increasingly reliant on HIV as its hepatitis C franchise slows (see tables below).

Bictegravir vs dolutegravir

The phase II study, presented today at the Conference on Retroviruses and Opportunistic Infections in Seattle, compared bictegravir plus emtricitabine and tenofovir alafenamide – known as FTC/TAF – with dolutegravir plus FTC/TAF in 98 treatment-naive, HIV-infected adults.

Both are the latest iterations of the integrase inhibitor class, and unlike older products with the same mechanism do not require boosting – taking another drug to raise circulating levels – so have a lower risk of adverse events and drug-drug interactions.

The phase II trial found similar response rates with a bictegravir-containing regimen versus a dolutegravir-containing therapy, which should boost confidence in Gilead’s compound ahead of phase III readouts expected mid-year.

It found a 97% response in the bictegravir arm at 24 and 48 weeks, versus 94% at week 24 and 91% at week 48 in the dolutegravir arm, but the difference was not statistically significant. Bictegravir also performed well on another important measure, viral resistance, with no cases observed. Gilead did not say whether resistance was seen in the dolutegravir arm.

Gilead will hope that the suggestion of a more favourable renal safety profile could help it set bictegravir apart from dolutegravir. But, on the flipside, a patient in the bictegravir group discontinued after a case of hives. No doubt investors will be keeping an eye on the side-effect profile in phase III.

If the ongoing phase III studies are positive Gilead plans to file for approval of a single-tablet regimen comprising bictegravir plus FTC/TAF in the third quarter.

Glaxo fights back

On the earleir call Glaxo's Mr Witty seemed unperturbed about bictegravir’s potential market entry, saying: “Clearly if a competitor brings out another product it just depends how good that product is. But at the very least you'd expected it to probably self-cannibalize some of its own portfolio.”

He pointed to dolutegravir’s “extraordinarily effective” resistance profile, concluding: “I think it's a pretty safe bet that the integrase market size grows.”

EvaluatePharma's consensus forecasts suggest that Glaxo will maintain its edge with its dolutegravir-based triple, Triumeq, in the coming years. And the company believes that it has another ace up its sleeve in the shape of the single-tablet doublet containing dolutegravir and Johnson & Johnson’s Edurant.

The outlook below does not include forecasts for a dolutegravir doublet, which, if it is as successful as Mr Witty believes, could change this picture of the future of the HIV market.

HIV market forecasts			
		Global sales ($m)	
Product	**Company**	**2016**	**2022**
Triumeq (dolutegravir-based triple)	Glaxosmithkline	2,217	4,698
Genvoya (elvitegravir-based quad)	Gilead Sciences	1,484	4,507
Descovy (emtricitabine-based doublet)	Gilead Sciences	298	3,393
Bictegravir/F/TAF (bictegravir-based triple)	Gilead Sciences	-	2,659
Odefsey (triple)	Gilead Sciences	329	2,348
Tivicay (dolutegravir monotherapy)	Glaxosmithkline	1,284	2,111
Isentress (raltegravir monotherapy)	Merck & Co	1,387	1,062
Prezista (darunavir monotherapy)	Johnson & Johnson	1,851	917
Edurant (rilpivirine monotherapy)	Johnson & Johnson	573	872
Vemlidy (tenofovir monotherapy)	Gilead Sciences	3	863
Total HIV market, incl others		**24,098**	**28,386**
Source: EvaluatePharma			

Glaxo presented more detailed data on the dolutegravir doublet phase III Sword 1 and Sword 2 switching studies at the CROI meeting, which it first toplined in December.

A pooled analysis of the trials found that 95% of patients achieved HIV-1 viral suppression at 48 weeks, and that the doublet was non-inferior to three and four-drug regimens. The company plans to submit the doublet for approval this year, meaning that it could be on the market a year from now, Leerink analysts estimate.

Potential concerns with a two-drug regimen include the durability of virologic suppression and resistance; Gilead will be watching to see if the dolutegravir doublet slips up here. But if these problems do not emerge Glaxo will be first to market with an appealing offering for an HIV population that is living longer and demanding a lower incidence of side effects.

Project	Study	Trial ID	Primary completion
Bictegravir	Phase II head-to-head trial	NCT02397694	Reported
Dolutegravir	Sword 1	NCT02429791	Reported
Dolutegravir	Sword 2	NCT02422797	Reported
Bictegravir	Phase III trial of bictegravir/emtricitabine/tenofovir alafenamide vs abacavir/dolutegravir/lamivudine	NCT02607930	May 2017
Bictegravir	Phase III trial of bictegravir/emtricitabine/tenofovir alafenamide vs dolutegravir + emtricitabine/tenofovir alafenamide	NCT02607956	May 2017
Bictegravir	Phase III switching study	NCT02603107	May 2017
Bictegravir	Phase III switching study	NCT02603120	Apr 2017
Bictegravir	Phase III switching study	NCT02652624	Sep 2017

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