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Glaxo doubles down in HIV

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Glaxosmithkline's bold step into the world of HIV doublets has been given a boost by two successful phase III trials. But, with its announcement containing little more than the top-line win, competitors in this field will be eager to see more details.

The main rival is of course Gilead, which has put everything into a triplet strategy that is expected to be extremely successful. At the same time, forecasts suggest that many remain to be convinced about Glaxo's two-drug products, and the company needs to quash concerns about viral resistance for this to change (see table below).

Forecasts illustrate the change in 2022 expectations for Glaxo and Gilead's novel doublet and triplet products since the beginning of this year. This shows that sellside analysts expect the US biotech's offering to become substantially more successful than Glaxo's, commercially speaking. This has much to do with the HIV field's comfort with multi-drug regimens, and physicians and patients will need convincing before readily cutting back on antiretroviral therapies.

The doublet-triplet wars

Company	Product	2022e sales ($m)	Change in forecasts YTD ($m)
Gilead	Biktarvy (bictegravir & emtricitabine & tenofovir)	4,994	(59)
Glaxo	Triumeq (dolutegravir & lamivudine & abacavir)	4,467	(711)
Glaxo	Dolutegravir & lamivudine	590	248
Glaxo	Juluca (dolutegravir & rilpivirine)	305	(271)

Source: EvaluatePharma.

Glaxo argues that HIV is essentially a chronic condition now and, because patients live longer and frequently develop other illnesses, reducing drug exposure is becoming increasingly important.

Of course this stance will only succeed if the group can show that a doublet is as effective as triple drug regimens at suppressing the HIV virus – and the Gemini trials unveiled today should go some way to establishing that.

Both studies were conducted in treatment-naive patients with a baseline viral load of less than 500,000 copies/ml, and found dolutegravir plus lamivudine to be non-inferior to a triple combination of dolutegravir, tenofovir and emtricitabine.

Tenofovir and emtricitabine are components of Gilead's triple Biktarvy. Notably, these studies do not test the double regimen against Glaxo's own triplet.

Resistance is futile

The only other information Glaxo provided today was that no patient who experienced virologic failure in either treatment arm developed treatment-emergent resistance.

What this might mean exactly is a crucial point. Presumably it refers to compliance. Non-compliant patients are more likely to see viral breakthroughs, which have been seen in previous studies and have prompted concerns that the doublet will only be suitable for certain patients (*Glaxo runs into double trouble in HIV, 27 July 2017*).

The non-compliant, and those with a higher viral load when treatment begins, are more likely to develop mutated forms of the HIV virus, which can become drug-resistant. By the sounds of Glaxo's statement this has not been seen, but a deeper look at the data remains crucial.

Glaxo is extremely optimistic about the potency of its dolutegravir-lamivudine doublet: the recruitment criteria for the Gemini trials were changed mid-study to include patients with much higher viral loads, who should be harder to treat.

Of course Gilead is equally convinced that it has the winning strategy, though its newly launched product Biktarvy disappointed in its first few months on the market. It is early days of course and the sellside expects triplets to remain dominant for the next few years at least.

Still, forecasts for the Glaxo doublet have been creeping up. Detailed data and the company's pricing strategy remain key unknowns. Perhaps equally important is Glaxo's ability to win over hearts and minds, in the inevitable headwind of a fierce campaign by Gilead to convince physicians and patients that in HIV three is better than two.

Study	Trial ID
Gemini 1	NCT02831673
Gemini 2	NCT02831764

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