Evaluate Vantage

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With Inlyta out of the picture, Votrient has first-line prize in its sights

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In the fast-shifting game of cat and mouse that is kidney cancer drug development, yesterday's phase III failure of Pfizer's Inlyta could give GlaxoSmithKline's Votrient a virtually unobstructed run at Sutent's dominance in the first-line setting.

Whatever crumbs of comfort Pfizer can salvage from the failure are unlikely to be of much use on their own given that the trial had compared Inlyta to Bayer/Onyx's Nexavar, which is now rarely used front line. Given Votrient's recent head-to-head success against Pfizer's Sutent – the most commonly used first-line drug – Glaxo looks to be sitting pretty, since a green light for Aveo Oncology's much-maligned tivozanib would represent a turn-up for the books.

Pfizer says in the Agile 1051 study Inlyta "narrowly missed" improving progression-free survival versus Nexavar, although it did show an undisclosed numerical increase that was driven by patients with good performance status. Full data have yet to be presented, but, whatever hope lies in the subgroup analysis, cross-study activity versus the more efficacious Sutent will be what interests the market.

Crowded field

Inlyta was approved for second-line use in the US and EU this year, joining a host of other drugs available for treating advanced renal cancer – Sutent, Nexavar, Votrient, Pfizer's Torisel, Novartis's Afinitor and Roche's Avastin (*Axitinib looks set to join competitive field for targeted kidney agents, December 8, 2011*).

Given how crowded this field has become, companies generally now view advancement to first-line use as the real prize. Inlyta's failure in this more lucrative setting prompted UBS analysts to remove an additional $250m in forecast US sales, with estimates now standing at a peak revenue figure of $350m in the US and $500m worldwide.

More immediately relevant is Glaxo's Votrient, which earlier this month hit the primary endpoint of showing non-inferiority to Sutent in terms of median progression-free survival, in the first-line Comparz study. Numerically Votrient actually performed slightly worse than Sutent, but this fell just within the predetermined definition of non-inferiority in hazard ratio terms.

Glaxo has yet to reveal any new commercial plans for Votrient, but success in Comparz points to an aggressive battle against Sutent in the first-line setting – a battle that will be easier if Inlyta moves out of the frame.

The Aveo wild card

Of course, there is still Aveo's tivozanib. Like Inlyta, this had been tested head to head against Nexavar, but unlike Inlyta it worked. However, although tivozanib was superior to the Bayer drug the result disappointed because analysts had wanted it to better the real-world first-line agent, Sutent, and based on historic data it did not (*Aveo's kidney cancer candidate looking weaker,August 06, 2012*).

The FDA's subsequent concerns over the overall survival trend seen in this study did nothing to restore confidence, but Aveo ploughed on undeterred and filed tivozanib – for first-line use – late last month. Shares in the Massachusetts-based biotech, whose project is partnered with Astellas Pharma, are down 52% since the start of the year.

None of which should pose much of an immediate concern to Pfizer, the Inlyta failure notwithstanding. The real market will be determined at least as much by selling muscle and drugs' side-effect profiles as efficacy.

Although it would have been nice to move Inlyta to front line, with Sutent and Torisel Pfizer has this field pretty much sewn up for now.

Phase III head-to-dead studies in renal cell cancer		
Study	**Detail**	**Trial ID**
Agile 1051	Inlyta vs Nexavar, 492 patients	NCT00920816
Comparz	Votrient vs Sutent, 927 patients	NCT00720941
Tivo-1	Tivozanib vs Nexavar, 517 patients	NCT01030783

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