Even Steven

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One of the challenges of HIV treatment advocacy is to remain objective, or as much so as possible. Objective means fair. Objective means following the data. Objective means not allowing feelings to overwhelm facts.

Objectivity is an ideal, and as such is unattainable. The point is not to achieve objectivity, but to strive for it. The closer to objective that I stay in my work, the better work I do. Hopefully that work, and that objectivity translate to some tangible gain in our war against HIV/AIDS.

Objectivity can be an elusive quality. This is particularly true when one very much has a ?dog in the fight.? Like anyone living with HIV, I am intensely vested in what happens in the research world. I want good drugs to succeed, in part because I need them to.

I am also subject to the ?wow factor.? I can be dazzled by data, star-struck by statistics. I am so immersed in the mostly mundane world of incremental improvements, when something sparkles I sit up and take notice. There is a fine line between being duly impressed and going ?coo-coo for coco puffs.?

As human as anyone, the trick for me is to self correct. I need to always want to pull back the curtain, and expose the man behind it. This might be a good time for some self-correction. I fear that I have been unfair- to a little molecule called maraviroc. Moreover, I think it is due, in part to being bedazzled by another molecule- raltegravir.

A little back story might help. A few years back, there were three CCR5 drugs close together in development- GSK aplaviroc, Schering?s vicriviroc and Pfizer?s maraviroc. Then came the train wreck. First, GSK announced they were halting development of aplaviroc due to rare, but serious liver toxicities. Soon after we heard that a woman in a trail of maraviroc needed a liver transplant (turned out it was not related to maraviroc). Soon after that we learned of higher rates of cancer seen in people taking vicriviroc than placebo in those studies.

Close to this time, we were getting our first real look at raltegravir. Companies had been unsuccessfully trying to develop integrase inhibitors for a long time, and many of us (or at least I) thought that Merck?s program was failing, simply because we hadn?t heard anything for a long time.

Not so much. Merck was sitting very quietly on their data, waiting to share it until just the right time. They went around showing treatment activists their early study results, and they were stunningly good.

Fast forward to 2006, as both maraviroc and raltegravir have clear paths to approval. Both are in phase III- the final phase before approval- and looking pretty good. I had the chance to meet fairly regularly with both companies, both individually and as part of advisory committees or other groups.

There was a subtly different tone between meetings with Merck and Pfizer. With Pfizer, there was much more of a focus on the potential for adverse effects. There was the fear of the drug causing a dangerous shift to X4. There was fear- based on animal studies- that blocking R5 could leave people more susceptible to certain viral infections. And then there was the fear of the unknown- this was after all the first and only HIV treatment that targets a component of the immune system rather than the virus. With Merck, we did talk about side effects, but there was less energy behind it. More focus was put on measures of efficacy, and the continued best-ever study results.

I understand the level of anxiety we had about R5 drugs, like maraviroc. The truth is, so far we haven?t seen the problems that we expected to, or at least worried about. What surprises me is that we weren?t equally fearful of raltegravir, which seems to work inside the nucleus of the cell. I should emphasize, we haven?t seen much in the way of problems with raltegravir.

Overall, I think the net effect was that we- or at least I was unfair to maraviroc. The data on maraviroc aren?t quite as spectacular as raltegravir- but there are what we call confounders (mostly the studies of raltegravir allowed the use of Prezista, where the maraviroc studies didn?t). Both drugs are powerful and well tolerated. The main downside of for maraviroc is the need for an expensive, time consuming test to see if you can even take it.

It is no secret that maraviroc sales have been slow. I don?t think that the community?s anxiety about the drug is to blame- I think it is mostly a lack of clear understanding of its best use. Still, I think that had maraviroc come to market earlier, it would have looked better, and more people would be taking it. It isn?t so much the molecule as when and how it came to market.

For my part, I will strive to do better next time- to be vigilant against the dazzle of data.
