EDITORIAL

Crossing the Line: Part 2

In a prior editorial we lauded the interactions between physicians, scientists, and industry that resulted in such breakthroughs as fluoxetine and lithotripsy, but lamented the fact that sometimes the same thought leaders "crossed the line" when, after launch, they worked with individual companies as subliminal salesman for the products they helped to develop.

Industry, too, sometimes crosses the line when they promote a treatment that they know (or suspect) may be inferior to or less safe than a competitor product. Merck has been accused by the lay press, tort lawyers, and others of doing just that with Vioxx (rofecoxib), its blockbuster Cox 2 inhibitor, but the facts, if there are such things, are less compelling than the rhetoric.

Rofecoxib was introduced to the marketplace in 1999 with much fanfare for the treatment of arthritis and pain. Prior to that, it had been well documented that 2%–4% of patients taking non-steroidal anti-inflammatory drugs (NSAIDS) for 1 year develop serious gastrointestinal complications (bleeding and perforation). Of those, about 15% die. Those with prior bleeding episodes are 10 times more likely to have serious GI complications. About 80% of patients with these serious complications are asymptomatic, including those that prove to be fatal! In head to head trials with other NSAIDS, Vioxx significantly reduced these GI complications by well over 50%.

In early October 2004, Merck voluntarily withdrew Vioxx from the market after a 2,600 patient phase 4 study demonstrated a doubling of the MI and stroke risk compared to placebo. After 18 months of continuous treatment, 25 patients taking placebo and 45 taking rofecoxib suffered a serious cardiovascular event. Prior Merck studies had also shown a higher rate of cardiovascular events and this was well documented in the package insert. The information was available to anyone who took the trouble to read.

To some extent, though, it was all in the fine print. Industry generally does not go out of its way to emphasize the shortcomings of the products it markets.

It seems very clear then, that for patients at risk for GI complications, Vioxx is, indeed, a worthwhile drug and for those not at risk, it might not be worth the extra cardiovascular risk. Risk versus benefit. That is part of the art of medicine. So, what is the problem?

The problem is that approximately 65% of the patients taking Vioxx were not at high risk for GI complications.

Why would that be?

Lack of knowledge by physicians and patients. Hype and advertising. Newer is better. These things are hard to measure, but a study by an economist came up with a very different conclusion. Patients with third party prescription coverage were twice as likely to use Vioxx, irrespective of GI risk, compared to those who paid out of pocket. But for those without coverage, use of Vioxx increased proportional to GI risk.

So who's at fault?

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