Adieu, Rimonabant

Failure of weight-loss drug was foreseen by Pro-Cannabis MDs

In November 2008 the European Medicines Agency (EMEA) has ordered Sanofi-Aventis to stop selling Rimonabant, a drug that reduces appetite by blocking cannabinoid receptors in the brain. Some 700,000 people have taken Rimonabant, which was marketed in the UK and elsewhere as Acomplia.

Data from ongoing clinical trials showed that Rimonabant users suffer depression, anxiety, insomnia and aggressive impulses at twice the rate of subjects given placebo. In one study there were five suicides among Rimonabant users compared to only one among subjects on placebo. On Oct. 23 the EMEA said “Enough” in 12 languages.

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Earlier in October Merck had abruptly canceled five clinical trials of a cannabinoid-blocker called Taranabant. The pattern of adverse psychiatric effects had become too obvious to conceal from U.S. and European regulators.

Unpublished to date are adverse effects involving cancer, seizures, and other illnesses that the cannabinoid system plays a role in suppressing. (In August researchers at the MD Anderson Cancer Center reported that mice on rimonabant develop potentially cancerous polyps at a higher rate than controls.)

The dangers of drugs that block cannabinoid receptors were foreseen by California doctors who monitor cannabis use by large numbers of patients. Jeffrey Hergenrather, MD, of San Francisco, was first to pub- licize his misgivings. Hergenrather had attended the 2004 meeting of the International Cannabinoid Research Society meeting at which Sanofi-Aventis researchers reported that Rimonabant had proven safe and effective in clinical trials involving 13,000 patients. That year the ICRS’s achievement award went to three Sanofi researchers and was presented by Raphael Mechoulam, the grand old man of the field. Many ICRSers got grants from Sanofi and/or the National Institute on Drug Abuse to study the potential of Rimonabant and other cannabinoid-antagonist drugs. Only a few expressed misgivings—off the record—about the basic approach.

Hergenrather and Dr. John MacPortland were lonely voices questioning the propriety of Sanofi’s march to the marketplace. “The consequences of interfering with the cannabinoid receptor system have not been evaluated in normal human physiology,” Hergenrather stated in O’Shaughnessy’s. He suggested that before Sanofi marketed Rimonabant, “It would be ethical to design longitu- dinal studies to assess the consequences of interfering with the cannabinoid system.”


Phil Denney, MD, saw a silver lining in Rimonabant and marketed it as a disease unto itself. The JAMA ad was one of about a dozen that Sanofi ran in medical jour- nals to explain Rimonabant’s mechan- ism of action. It said that the endocana- nabinoid system “consists of signaling molecules and their receptors, includ- ing the cannabinoid receptors (CB1 and CB2).” The CB1 receptors are “located centrally in the brain and peripherally in liver, muscle and adipose tissue” and “may assist in regulating physiologic processes, e.g., lipid and glucose me- tabolism.”

But the gusher of enlightenment that Denney anticipated shimmered outquick- ly. Sanofi did not succeed in defining “Metabolic Disorder” as a real disease and the way Eli Lilly had with “Clinical Depression.” A nation that had been educated about the serotonin reuptake process did not get equivalent instruc- tion about the cannabinoid receptor system. The information contained in the few medical-journal ads never crossed over into the mass media.

In most of the stories dealing with the rise and fall of Rimonabant, reporters avoided the term “cannabinoid recep- tor system” entirely. For example, in Jeanne Whalen’s Oct. 24 Wall St. Jour- nial piece about the EMEA withdrawing approval, she described Rimonabant as “a new kind of drug that blocks recep- tors in the brain that help control food intake.”

To those who suspect a conscious decision by Prohibitionist publishers to prevent the public from learning about the cannabinoid receptor system, we say: never underestimate the role of bone-ignorant journalists.

In March, 2007, when the FDA was evaluating Rimonabant, Whalen wrote a front-page piece with this doubly in- accurate phrase: “Cannabis, the active ingredient in marihuana, acts on the same receptors…”

I wrote a polite note to the editor explaining that “cannabis” and “mari- juana” are synonyms, and that the plant contains more than one active ingredient. Ms. Whalen emailed back: “Thanks for writing—always good to hear from readers. I actually didn’t mean to get that technical in my pre- sentation. I was really just saying that the drug marihuana is made from cannabis. But thank you for the points you make. Best regards, Jeanne Whalen.”

This woman covers the European pharmaceutical industry for the Wall St. Journal! Has any honor accrued to Hergenrather and the SCC doctors who joined in warning that Rimonabant would in- duce serious adverse side-effects? Of course not—they are “potdocs.” Her- genrather spent part of this past week-end drafting a letter to a Butte County judge who won’t allow a patient of his to medicate with cannabis while on probation unless the patient gets a sec- ond approval from an orthopedist.

The patient is a middle-aged construction worker with a well-documented history of back pain for which he has been hospitalized, treated by chi- ropractors, acupuncturists, osteopaths, and physical therapists, and prescribed Celebrex, Flexeril, Soma, Valium, Vi- codin, Percodan, Percocet, Darvocet, Ultram, ibuprofen, naproxen, etc.

Not only is the judge playing doc- tor, she doesn’t understand that ortho- pedists have no expertise treating pain. Dr. Hergenrather put this much more diplomatically in his letter to her—as diplomatically as he put his warning about Rimonabant to the distinguished pharmacologists in the summer of 2004.