

Recent Drug Trials Offer Hope



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Research on therapeutic interventions for CFS all too often focuses on behavioral remedies. Researchers, universities, the biotech industry and pharmaceutical companies must explore more drug interventions for CFS patients.

AT-A-GLANCE ►►

- Here's a look at three clinical trials of medications that may be helpful in treating CFS, at least in some subsets of patients.
- The medications being studied are currently manufactured under the brand names Procrit, Valcyte and Valtrex. They are FDA-approved for other medical conditions.

During the past two decades most CFS research has focused on detecting the cause or causes of the illness rather than on treatment options. While it's vitally important for researchers to continue to explore etiology to unravel the pathogenesis and uncover biomarkers, patients who are suffering need relief *now* while they wait for researchers to discover what causes CFS.

There has yet to be a single drug developed and approved for treating CFS. While there are a number of drug interventions that are useful in ameliorating symptoms, there is a great need for drug companies, biotech firms and researchers to focus on new treatments for CFS, an illness that affects more Americans than multiple sclerosis, lupus or ovarian cancer. That's why it was heartening to hear news at the IACFS conference in January 2007 of various clinical trials currently under way that focus on pharmacologic therapies for CFS. Let's take a brief look at three of these studies.

Miami's Epoetin Alpha Clinical Trial

Many investigators now believe there may be multiple triggers or causes for CFS, and a significant body of research is focused on identifying subsets of patients and employing those subsets in future research studies. Categorizing CFS patients by subgroup may also be extremely valuable in research on treatments. If the pathogenesis of the illness varies from one group to another, it's entirely possible that treatments will also need to vary. What works for one group of CFS patients may not necessarily work for another group.

According to Barry Hurwitz, PhD, the need to categorize patients by subset may explain, in part, why there are so many null findings in clinical trials conducted so far in the CFS research field. Hurwitz, who made this remark during his presentation at the IACFS conference, added that lack of placebo controls, lack of uniformity in outcome measures, the waxing and waning of symptoms and other factors have also contributed to the disappointing lack of definitive answers. In any case, Hurwitz concludes that it's essential to enhance the homogeneity of cohorts if researchers are to make progress in clinical trials.

In an attempt at just this kind of homogeneity, Hurwitz and his team at the University of Miami have been conducting a clinical trial of a subset of CFS patients who exhibit diminished red blood cell volume (RBCV) to determine if epoetin alpha (Procrit) has any effect on fatigue, orthostatic problems or RBCV.

The 54 CFS patients (of 104 screened) in the study included 36 with low RBCV and 18 with normal RBCV. Patients with low RBCV were randomized to

either epoetin alpha or placebo treatment, and patients with normal RBCV received placebo treatment over a four-month period. To determine orthostatic susceptibility, a head-up tilt test was performed.

Results presented at the conference indicate that epoetin alpha treatment in the subgroup of CFS patients with low RBCV induced a significant increase in blood volume, raising it to a level consistent with the normal group. However, fatigue didn't appear to be diminished or influenced by the drug treatment, and susceptibility to orthostatic syncope was reduced more in subjects who displayed greater improvement in RBCV after treatment.

Stanford's Pilot Trial of Valganciclovir

Jose Montoya, MD, of Stanford University's School of Medicine, presented research on the effect of valganciclovir on CFS patients. Again, the research focused on a subset of patients—those with very high levels of antibodies for human herpes virus 6 (HHV-6) and for Epstein-Barr virus (EBV). Montoya says he and his colleagues believe “the two viruses working together are creating and maintaining the disease.”

During the past three years Montoya's team has treated 25 CFS patients with valganciclovir—specifically with a new oral form of the drug. However, the paper presented at the conference only included a cohort of 12 patients.

The cohort was treated with the antiviral drug for six months. After an initial worsening of symptoms, 9 of the 12 patients, or 75 percent, reported significant improvement in symptoms. Fatigue lessened, enlarged lymph nodes shrank, energy levels increased and overall activity levels improved. Interestingly, only patients who reported the onset of CFS following severe flu-like symptoms improved with this drug treatment. And improvement was sustained even months after going off the medication.

The study results were promising enough for Roche Pharmaceutical to award Montoya a \$1.3 million grant to conduct a randomized, placebo-controlled, double-blind study at Stanford. Roche manufactures the drug valganciclovir under the brand name Valcyte. The study will focus on the same subset of CFS patients, those who have viral-induced dysfunction of the central nervous system.

Valcyte is FDA-approved for the treatment of other medical conditions, so it's currently available. However, the study's researchers and CFS clinicians are advising caution about off-label use at this time. The study is small and preliminary, and it needs to be confirmed with the larger study at Stanford. Also, the side effects of Valcyte can be

significant and toxicity has to be carefully monitored; adverse renal effects aren't uncommon. The drug is also expensive, about \$2,000 a month in the U.S.

Testing Two Antiviral Therapies

Martin Lerner, MD, presented results of another study of antiviral therapy for chronic fatigue syndrome. This study included both valganciclovir (Valcyte) and valacyclovir, which is manufactured by Glaxo Wellcome under the brand name Valtrex.

Lerner, an attending physician at William Beaumont Hospital and a clinical professor at Wayne State University School of Medicine, noted that patients with CFS frequently exhibit evidence of infection with Epstein-Barr virus and/or cytomegalovirus (HCMV). Consequently, he said, the “paradigm guiding this research is that persisting infection with one or both of these viruses may be etiologically related to CFS.”

This Phase I clinical trial divided study participants into three CFS subgroups. The first group included 27 patients with EBV antibodies who were administered valacyclovir for 6 months and another 27 CFS patients who were administered a placebo for 36 months. The second subset included only a single patient with EBV and HCMV coinfection who was treated with valganciclovir for 42 months. The third group of 9 patients with EBV and HCMV coinfection were treated with both drugs for 30 months.

Although the trial cohort is relatively small, the study duration was notable in trying to determine if the long-term use of a single antiviral or a combination of two antiviral medications could achieve positive results with a subset of CFS patients. The study authors reported that “with valacyclovir and/or valganciclovir, sinus tachycardias at rest lessened, abnormal cardiac wall motion improved, and EBV viral capsid antigen and IgM serum antibodies diminished.” They also reported a reduction in symptoms, including sore throats, fevers, syncope, chest pain and muscle aches.

While FDA marketing approval for use of these medications for CFS is still uncertain, and won't occur soon even if larger trials prove their efficacy, the results are encouraging and worthy of further exploration. This also may signal

a long overdue interest in CFS as a “market” for pharmacologic treatments, which may accelerate progress in patient care. ■

