Informed Consent: Valcyte (valganciclovir) Treatment for Chronic Fatigue Syndrome

From Richard Podell, M.D., MPH, August 3, 2014

Background:

Currently there are no proven effective treatments for chronic fatigue syndrome (CFS).

Most experts strongly suspect that Herpes Class viruses such as Epstein Barr Virus (EBV), HHV-6, and/or Cytomegalovirus (CMV) play an important role for some but not all CFS patients.

Several leading CFS specialists offer selected patients the option of long-term anti-viral treatment with valganciclovir (brand name, Valcyte). These physicians include Jose Montoya, M.D., professor of infectious disease at Stanford Medical School and Andreas Kogelnik, M.D., Director of the Open Medicine Institute, Mountain View, California.

Drs. Montoya and Kogelnik and other CFS specialists also offer selected patients treatment with several anti-virals including Valtrex and Famvir. These are currently used to treat Shingles and/or Herpes Simplex Virus.

At this time we have only one very well done double blind study evaluating a six month long course of Valcyte as a treatment for Chronic Fatigue Syndrome. This study was done at Stanford. Although the results were somewhat encouraging, they were not conclusive. Partly this may be due to the study’s small size—only 20 patients treated with Valcyte and 10 with placebo.

A report on the Stanford study can be found at this site: http://onlinelibrary.wiley.com/doi/10.1002/jmv.23713/full

Valcyte is currently FDA approved only to treat CMV infection for persons with AIDS or with organ transplants. It is not FDA approved to treat chronic fatigue syndrome or to treat other viruses.

Leading experts believe that Valcyte may be more effective than Famvir or Valtrex for Epstein Barr and HHV6 viruses. However, this is not certain. Also,
Valcyte is more expensive, more difficult to obtain insurance coverage for, and may be likely to cause more side effects compared to Valtrex or Famvir.

Until more studies are available I prefer to offer Valtrex or Famvir as first choice rather than Valcyte. However, I am willing to offer Valcyte for selected patients—if they fully understand the very limited data on which this treatment relies, the potential for toxicity, the potential costs, and the need for very close and careful monitoring of both clinical status and laboratory tests.

Currently, most CFS specialists prefer to treat only those CFS patients who have very high levels of antibodies against Epstein Barr and/or HHV-6 and/or CMV virus. They tend to not treat patients whose antibody levels are only mildly or moderately high.

Unfortunately, we currently lack laboratory tools to clearly distinguish between latent, inactive herpes-class viruses versus an active recurring infection. (Herpes class viruses stay in the body for life, so many or most of us have antibodies against them. For example, chicken pox is a herpes virus, which—after the initial infection-- can remain latent throughout life. Or it can reactivate and cause the disease we know as shingles.) Until, we have better tools, it is likely that we may be over-treating certain patients and under-treating others.

**Eligibility for Valcyte Treatment Protocol:**

Must have chronic fatigue syndrome

Must have relatively high antibody levels to Epstein Barr Virus and/or HHV-6 virus, and or CMV virus. Please note: Insurance coverage is only a possibility if CMV antibody levels are high. Even then insurance coverage may be difficult to obtain. Self Pay is possible. However Valcyte is very expensive, even as a generic.

Must be between ages 21 and 60.

Must not be pregnant or lactating or planning to become pregnant during the next 12 months/ Men must use barrier contraceptives during treatment and for at least 90 days after stopping treatment.
Must have normal kidney function.

Must fully understand that treatment with Valcyte is a non-standard non-FDA approved treatment with significant potential risks.

Must have adequate home support available. Reason: patients in Dr. Montoya’s Valcyte study often became worse before they improved. In the Stanford study many of the patients who eventually improved became worse during the first two months of treatment. We will be using a lower initial dose compared to the Stanford study but initial worsening might still occur.

Must intend to continue treatment for six months or more if the treatment is tolerated.

Must be willing and able to comply with medical and laboratory monitoring. Laboratory monitoring will require monthly blood and urine tests. Medical visits will be monthly. Longer intervals might be considered if patient is doing well.

Patients must have the financial resources to maintain Valcyte therapy for at least six months. However, treatment, if favorable would likely last longer.

Before starting Valcyte patients and supervising clinicians should read the entire FDA approved Valcyte Package Insert. This is available online at http://www.accessdata.fda.gov/drugsatfda_docs/label/2001/21304lbl.pdf

The following is a brief and only partial summary of information from the drug package insert. Patients should ask the physician any and all questions that may arise at any time before or during their treatment.

**FDA approved Indications:** Valcyte (valganciclovir) is FDA approved only for treatment of CMV virus in the context of HIV or organ transplants. It is not FDA approved for Chronic Fatigue...
Syndrome or to treat Epstein Barr Virus, HHV-6 or any virus other than CMV.

**Warnings:** Valcyte can cause dangerous decreases in the level of white blood cells, red blood cell count, and platelets. Such changes can increase vulnerability to severe or fatal infections, anemia and/or bleeding.

*Valcyte can cause cancers in animals. It is not known to what degree Valcyte might be carcinogenic in humans.*

In animals Valcyte inhibits the production of sperm. These changes were reversible at low doses but permanent at high doses. Men taking Valcyte should practice barrier contraception for at least 90 days following treatment with Valcyte.

Valcyte can cause mutations. Women must use effective contraception during Valcyte treatment and for some time after stopping. Animal data indicates that suppression of fertility in females may also occur.

Valcyte is contraindicated for patients who allergic to valganciclovir or ganciclovir.

**Kidney Function:** Valcyte is eliminated from the body mainly through the kidneys. Valcyte clearance from the body is reduced. This increases the level of Valcyte in the blood. The FDA approved drug package insert recommends that the dose of Valcyte be reduced if kidney function is decreased. However, our protocol will exclude patients who have abnormal kidney function.

Side-effects: Among patients with AIDS or organ transplant and CMV infection, significant laboratory abnormalities and side effects were very common. The most common side effects were diarrhea, nausea, low white blood cell count, headache, fever, anemia, insomnia, and peripheral neuropathy. Serious adverse reactions included bone marrow and blood count depression, reduced kidney
function, major infections, bleeding, convulsions, confusion, and hallucinations.

*However, patients with chronic fatigue syndrome appear to tolerate Valcyte much better than those who have AIDS or organ transplant.* In the Stanford study and in the subsequent clinical experience of Dr. Montoya and Dr. Kogelnik, significant laboratory abnormalities and serious side effects were infrequent. Nevertheless, potentially serious adverse reactions must still be considered.

**Other:** Valcyte should be taken with food.

No drug interaction studies have been done on Valcyte. However, it is expected that Valcyte (valganciclovir) will have similar interactions to that of the closely related drug, ganciclovir.

**Dr. Podell’s Current Treatment Protocol:**

*Step I:* Medical Evaluation to assure that the diagnosis of chronic fatigue syndrome is satisfied, and that there are no contraindicating co-existing health problems. Pre-treatment lab tests will include CBC, CMP, urinalysis; Epstein Barr Virus, HHV-6 and CMV antibody levels. Other tests will be as medically indicated. In some cases we will require a 24 hour urine and blood test for creatinine clearance.

*Step II:* Start Valcyte (brand or generic) at 450 mg once daily for one to four weeks. If tolerated, dose will be increased to 450 mg twice daily for six months or longer. Please note, the Stanford study started with 900 mg twice daily for the first 3 weeks and then 450 mg twice daily afterward. My protocol will start with a lower dose and not go higher than 450 mg twice daily.

*Step III:* CBC, CMP and urinalysis will be required monthly. Initially, medical visits will be monthly. For persons doing well the visit schedule might become less frequent. However, monthly lab s will continue. Antibody levels to Epstein Barr, HHV-6 or CMV will be done at intervals.