



COUNTY OF SONOMA
DEPARTMENT OF HEALTH SERVICES

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From: Leigh Hall, MD
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Date: May 23, 2005

Subject: Available West Nile Virus Randomized Control Treatment Trials
for your Patients

Attached is information about three investigational treatment trials for neuroinvasive disease caused by West Nile virus. Though there is no known treatment for West Nile virus neuroinvasive disease, these trials may be available for your patients.

The Sonoma County Department of Health Services is expecting the first cases of West Nile virus in the county to appear this summer, including the probability of some neuroinvasive disease.

The contacts for enrollment of patients are included in the attached information. Please also feel free to call me at 565-4599 with any questions.

May 11, 2005

Available West Nile Virus Randomized Control Treatment Trials in US – 2005

- 1) A Randomized Double-Blinded, Placebo Controlled Trial of Alpha-Interferon (Alferon) Therapy for West Nile Meningoencephalitis (Protocol WN-102)
- 2) A Phase I/II Randomized, Placebo-controlled Trial to Assess the Safety and Efficacy of Intravenous Immunoglobulin G (Omr-IgG-am) Containing High Anti-West Nile Virus Antibody Titers in Patients With, or at High Risk for Progression to West Nile Virus (WNV) Encephalitis and/or Myelitis. Sponsored by: National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health
- 3) An Exploratory Study of the Safety, Tolerability, Pharmacokinetics and Potential Effectiveness of AVI-4020 Injection in Patients Presenting with Presumptive Acute Neuroinvasive West Nile Virus (WNV) Disease

WNV Treatment Trial #1: Interferon

Background

- Interferon alpha-2b
 - Used to treat Hepatitis C (related virus)
- In vitro:
 - Interferon alpha-2b inhibited replication at relatively low concentrations
- Animal studies:
 - Increased mean survival time of SCID-treated mice infected with related flavivirus
 - Reduced viral RNA in serum, brain and spleen
- Proposed Mechanism
 - Stimulates cellular antiviral activity, enhances body's host defenses (anti-viral replication has also been proposed as mechanism of action)
- Study of SLE patients found benefit with early initiation of interferon: decreased severity at 3 weeks (non-randomized, not blinded, historic controls) [J Infect Dis 2004, 190:1084-7]
- Pilot study 2002 and 2003 of WNV encephalitis [44th ICAAC presentation, Washington, Nov 04]
 - Randomized, not blinded, multi-center
 - N=15 Rx with Interferon alpha-2b x 2 weeks
 - N=8 usual supportive care

- Treated group had a significant improvement vs no Rx (based on mean change of the NIHSS at 3 weeks)
- Side effects interferon: reversible neutropenia, hepatitis

Trial

- Goal: enroll ~60 patients (3 enrolled to date)
- Randomized placebo-controlled, blinded study
- Interferon alpha-N3 will be used; better tolerated than IFN alpha-2b with less neutropenia, lymphopenia and fever

Contact Information

- James Rahal (JJR9002@nyp.org)
- Wehbeh Wehbeh (wew9004@nyp.org)

phone: (718) 670-1525

<http://www.nyhq.org/posting/rahal.html>

WNV Treatment Trial #2: IVIG

Background

- Omrix (Israeli company) partnering with NIAID;
 - Immunoglobulin that contains antibodies to WNV
 - Developed from plasma of Israeli donors with high level of antibodies to WNV
 - Goal to enroll 100 hospitalized patients > 18 years with WNV-related encephalitis
 - 3 groups: (3:1:1)
 - WNV-IVIG (Omr-Ig-am)
 - standard IVIG (from U.S.)
 - Placebo
- "dramatic response" to Omr-IgG-am; 70 yr old, immunocompromised patient*
- "rapid improvement"; 42 yr old lung transplant**
- ~6 other cases: 2 improved, 2 no change, 2 death^
- Prophylactic and therapeutic efficacy in treating West Nile virus in mice^^

*Emerg Infect Dis, 2001

**Transplant ID 2002

^J Infect Dis, 2003

Contact Information

- Laura Riser, CASG Clinical Administrator,
University of Alabama
(205) 934-2424 (lriser@peds.uab.edu)
- Penny Jester, CASG Project Manager,
University of Alabama
(205) 996-7800 (pjester@peds.uab.edu)

<http://www.clinicaltrials.gov/show/NCT00068055>

WNV Treatment Trial #3: 3rd Generation Anti-sense

Background

- 3rd Generation Antisense compound AVI-4020;
 - Neutral charge (less toxicity)
 - Not degraded by serum and/or cellular degradative enzymes
 - Excreted unchanged via the urinary tract
- Interferes with WNV mRNA translation → prevents WNV replication
- Animal studies (rats/monkeys)
 - AVI-4020 distributes throughout the body, including across the normal blood-brain barrier
 - No safety or toxicity concerns at doses considered 20X therapeutic dose level
source of data: AVI BioPharma, Inc.
- AVI-4020-CL-01: Pilot Study in Summer/Fall 2003
 - Total of 10 volunteers received at least one dose of AVI-4020
 - 7 with active/recent/remote WNV disease
 - 3 with recent viral illness
 - No safety or toxicity concerns
» Source of data: AVI BioPharma, Inc.
- Emergency IND in June 2004
 - MD request for active WNV neuroinvasive disease (polio-like syndrome) in June 2004
 - AVI-4020 administered intravenously at 45 mg Q12 hours x 5 days
 - No safety or toxicity concerns at this dosage level
 - AVI-4020 drug levels in CSF were determined:
 - ~3 times higher than when 15 mg Q12 hrs administered
 - Considered sufficient to interfere with WNV translation based on a cell free assay
 - Dramatic resolution of meningitis and eventual full neurologic recovery within 2

months

Source of data: AVI BioPharma, Inc.

Contact Information

- Phone contact: 503-227-0554
- WNV response team: 800-225-8101
 - Dr. Peter O’Hanley, Sr. VP Clinical Development
 - Desiree Hollemon, Director Clinical Operations (DHollemon@avibio.com)
 - Janet Christensen, VP Quality Assurance and Regulatory Affairs

<http://www.clinicaltrials.gov/ct/show/NCT00091845>