Medscape Conference Coverage, based on selected sessions at the:

XVII European Stroke Conference

This activity is not sanctioned by, nor a part of, the European Stroke Conference. Conference news does not receive grant support and is produced independently.

Medscape Medical News

CLEAR Result: Low-Dose tPA Safe, Effective in Treating Intraventricular Hemorrhage

Caroline Cassels

May 15, 2008

May 15, 2008 (Nice, France) — Treatment of intraventricular hemorrhage (IVH) with catheter-based clot lysis using low-dose tissue plasminogen activator (tPA) is safe and dramatically reduces death and disability in individuals with this usually lethal condition.

Here at the 17th European Stroke Conference, investigators presented the final results of the Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage (CLEAR-IVF) trial, showing that administration of 1-mg tPA every 8 hours to a maximum of 4 days reduced expected mortality by approximately 70% and resulted in a dramatic improvement in functional outcomes.

"At 30 days, the mortality rate in study subjects was 15%. Typically, the expected 30-day mortality in such patients is about 80% to 85%," study

Editors' Recommendations

Mobile Stroke Unit Cuts Time to Treatment

The PROFI Study (Prevention of Cerebral Embolization by Proximal Balloon Occlusion Compared to Filter Protection During Carotid Artery Stenting)

Do Contrast Agents Impede Clot-Busting Drugs in Ischemic Stroke Patients?

Drug & Reference Information

Carotid Artery Stenosis Imaging

Vertebrobasilar Stroke

Most Popular Articles

According to PHYSICIANS

1. OTC Supplement May Aid in Migraine Prevention
2. Lifestyle and Burnout: A Bad Marriage
3. Green Tea, Coffee May Guard Against Stroke
4. Azithromycin Poses Fatal Cardiac Risk, FDA Warns
5. Are You a Great Diagnostician?

View More

investigator Daniel F. Hanley, MD, told *Medscape Neurology & Neurosurgery*.

However, he added, the "real news" is that fact that over 30, 90, and 180 days, more than 40% of patients recovered to the point that they were able to live independently, a result that Dr. Hanley described as "phenomenal."

"With this type of devastating disease, there is always the consideration that even if you can save lives, are patients paying a price in terms of their quality of life? In this study, 40% of our subjects recovered to the point of living independently, and 10% were completely normal with no deficits. The most recent patient I saw has now returned to work," he said.

Counterintuitive Treatment?

According to Dr. Hanley, while the idea of using thrombolysis to treat hemorrhagic stroke may seem "counterintuitive," he pointed out that over the past 15 years there has been a large number of published case series suggesting the use of tPA for IVH is feasible and likely safe.

However, dose effect and dose safety remained unclear as well as the treatment's potential impact on outcome. Dr. Hanley said the CLEAR-IVH trial is the first multicenter, international prospective assessment of this treatment.

Building on previous research showing that low-dose tPA did not increase bleeding risk and that the treatment is more effective if the catheter used to deliver the drug is placed closer to the clot, the researchers embarked on the current phase 2 study to determine the safest and most effective regimen.

Developed by Dr. Hanley and colleagues, the procedure clears trapped blood by bathing — and dissolving — the clot directly in tPA in a system that is closed for 1 hour to allow the drug to interact with the clot. The system is then opened up to facilitate drainage of lysed clot materials.

The study included 52 patients from 20 centers in the United States, Canada, the United Kingdom, and Germany. All subjects had a confirmed diagnosis of IVH via CT scan with third or fourth ventricle obstruction.

Six-Hour Stability Period Crucial

A second CT scan was performed 6 hours after catheter placement to ensure that there was no ongoing bleeding before administration of the drug.

"This six-hour stability period is necessary to make sure there is no bleeding. After dose, I believe this is the single most important component in determining the safe use of this drug in this [clinical] situation," said Dr. Hanley.

Subjects received 1 of 3 regimens — 0.3 mg of the drug every 12 hours, 1 mg of the drug every 12 hours, or 1 mg of the drug every 8 hours.

Patients were monitored with daily CT scans, and the investigators found that clots dissolved on average within 3 to 4 days. Study subjects who received the 1-mg dose every 8 hours experienced dissolution of their clots an average of 1 day earlier than their counterparts on the other 2 regimens.

The investigators found symptomatic bleeding occurred at a rate of about 6% — a rate that was the same as that found in the placebo group in the investigators' prior trial. "There was no enhanced bleeding as a result of the procedure," said Dr. Hanley. Other complications included a 2% rate of bacterial ventriculitis.

Worldwide Applicability

Because the procedure is relatively simple, uses currently available technology, and requires no special training, the CLEAR-IVH approach could easily be applied worldwide, said Dr. Hanley.

"It requires a CT scan, a neurosurgeon to place a catheter, and a proper

understanding of how to use a lower-dose thrombolytic. There's no particular special training required, although there are nuances in the daily reading of the CT scans," he said.

Despite these encouraging findings, Dr. Hanley said it is not yet clear whether this should be employed as a standard treatment for IVH, which affects about 50,000 Americans every year.

To answer this question, the investigators are planning a definitive, multicenter, randomized phase 3 trial that will include 500 patients and is expected to launch at the end of 2008 or early 2009.

"Our group is fully committed to testing the novel ideal that IVH clot-size reduction with thrombolysis decreases mortality and increases good outcome," said Dr. Hanley.

The study was supported by Johns Hopkins University, the FDA Office of Orphan Products Development, and Genentech.

17th European Stroke Conference. Presented May 14, 2008.





Cite this article: Caroline Cassels. CLEAR Result: Low-Dose tPA Safe, Effective in Treating Intraventricular Hemorrhage. *Medscape*. May 15, 2008.