Emergency treatment for devastating stroke to be tested in Memphis

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The University of Tennessee Health Science Center's Stroke Team is joining researchers from more than 100 hospitals worldwide to conduct a National Institutes of Health (NIH)-funded research study called FASTEST that will test the safety and efficacy of a medication called recombinant factor Vlla to prevent hemorrhage expansion in patients with strokes caused by bleeding in the brain—intracerebral hemorrhage strokes.

The study's local principal investigator is Anne Alexandrov, Ph.D., AG-ACNP-BC, RN, CCRN, ANVP-BC, NVRN-BC, FAAN, a professor in the UTHSC College of Nursing and chief nurse practitioner of the UTHSC Mobile Stroke Unit. Physicians from the UTHSC Stroke Team and the UTHSC Neurocritical Care Team are co-investigators on the study. FASTEST stands for rFVIIa for Acute Hemorrhagic Stroke Administered at Earliest Time.

Intracerebral hemorrhage occurs when a weakened blood vessel breaks because of extreme uncontrolled hypertension. It produces the most devastating of all strokes, with more than 40 percent of patients dying within the first 30 days and only 20 percent of patients able to return to an independent life after six months, Dr. Alexandrov said. Unfortunately for these patients, bleeding often continues to expand once it starts, and in about one-third of cases, the expansion will lead to devastating neurologic deterioration and death. Intracerebral hemorrhage accounts for about 10-15 percent of all stroke events nationally, according to the American Stroke Association. In the Mid-South, almost 300 patients

suffer this devastating form of stroke each year, according to UTHSC Stroke Team data.

There is currently no treatment for this condition that is capable of improving outcomes or stopping bleeding expansion. The UTHSC FASTEST study aims to test whether factor VIIa, a drug that is currently FDA-approved to treat hemophilia, will stop hemorrhage expansion and therefore reduce the risk of death and worsening neurologic outcomes. Hemophilia is an inherited condition where certain clotting factors are missing in the blood. Factor VIIa is a protein made in the human body to stop bleeding at the site of injury to a blood vessel.

Two sites in Memphis will be participating in the FASTEST study: Methodist University Hospital and the UTHSC Mobile Stroke Unit, Dr. Alexandrov said. The Mobile Stroke Unit offers the unique opportunity to treat patients very early outside the hospital in the ambulance once they have undergone a brain CT scan and been diagnosed with an intracerebral hemorrhage. This extremely early treatment is a great advantage to the patient and could prevent devastating bleeding expansion.

At times when the Mobile Stroke Unit is not in service, patients who are diagnosed in the Methodist University Hospital Emergency Department with an intracerebral hemorrhage may also be enrolled in the study. "The key to being selected for study enrollment is the time from onset of bleeding to diagnosis, with only those who arrive within two hours being considered possible candidates for treatment," Dr. Alexandrov said. After this period of time, it is likely that the damage has been done and significant hemorrhage expansion has already occurred, so late arrival disqualifies patients for enrollment in the study, she said.

Unique to the study is the "exception from informed consent" process that will be used. "Because patients with this type of stroke are often so

disabled that they cannot understand information or even respond to questions, we will enroll them without consent if we are unable to find a legal next of kin to provide consent for them," Dr. Alexandrov said. This approach is taken when the benefits of treatment outweigh the risks, so that every patient encountered has the best possible chance to prevent bleeding expansion.

"The longer we wait to find someone to consent for drug administration, the greater the likelihood that the hemorrhage is expanding and the patient will deteriorate, making the exception from informed consent process the most realistic approach," she said. Once the patient recovers or family members are available to provide consent for continuation in the study, the research team will explain the study and offer consent to continue participation in the trial. This alternative consent model is widely accepted in research involving cardiac arrest, trauma, and other conditions that place people at immediate maximum risk when they cannot speak for themselves and there is no time to wait for legal next of kin to become available to consent, she said.

Factor VIIa has been shown to stop bleeding, but in previous clinical stroke trials, patients were treated too long after the stroke had started to make a difference in their outcome. Because the drug produces clotting, there are some risks to use of the drug, including the risk of causing a clot to develop in other parts of the body, such as the heart or the lower extremities. Patients will be closely monitored for all reactions that may be harmful, and medical care will be immediately provided to treat any problems that arise, Dr. Alexandrov said. "What's most important is stopping the bleeding from expanding in the brain, because this is the primary cause of severe disability and death," she said.

The study is designed as a randomized, double-blind, placebo-controlled trial, whereby both the patients and the treating team do not know whether the real drug (factor VIIa) or the placebo (packaged identically)

is being administered. This is the highest form of clinical trial design, because it prevents bias in study interpretation. "Patients will be randomly selected by a computer to get either the drug or the placebo agent, but both the drug and placebo will look identical, so that neither the research team nor the patient/family knows which agent was given," she said. The method used for the study is similar to vaccine trials for COVID-19 that are underway around the world.

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