Transcript Details

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Comparing In-hospital Mortality With Andexanet Alfa Versus 4-Factor Prothrombin Complex Concentrate

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Fermann:
My name is Greg Fermann. I currently serve as Professor and Executive Vice Chair of Emergency Medicine at the University of Cincinnati. It's my pleasure to present the results of our study on behalf of the authorship group listed here comparing in-hospital mortality with induction and alpha versus 4-factor PCCs.

Factor Xa inhibitors such as rivaroxaban and apixaban effectively reduce the risk of ischemic events but also increase the risk of major bleeding. In 2018, the FDA approved andexanet alfa. Until that time, there was very limited ability for clinicians to manage such bleeding. Four-factor PCCs have been used off label to manage such bleeding. But there's a scarcity of data comparing these two strategies. So our objective in this trial was to compare the occurrence of in-hospital mortality in patients treated with either andexanet alfa versus 4-factor PCCs when they're hospitalized for either rivaroxaban or apixaban-associated major bleeding.

It was a multicenter observational cohort study, where we reviewed the electronic health record of over 350 U.S. hospitals with discharge dates from May 2018 to September 2022. These are adult subjects age of greater than 18. They were hospitalized for anticoagulant associated major bleeding, and were taking rivaroxaban or apixaban at the time of the bleeding event, and they were treated with either andexanet alfa or 4-factor PCCs. What did we collect? Well, we collected patient and treatment characteristics. We looked at patient demographics and comorbidities, the factor Xa inhibitor administration, time since last anticoagulant dose, and the type of factor Xa inhibitor. We also asked the subjects for bleeding location, cause, and severity. The location of bleed, ICH versus GI versus critical compartment, whether or not it was traumatic or spontaneous. We tried to assess for ICH severity using GCS as a cohort parameter there, and then also GI bleeding location, upper, lower, both, or unavailable.

Our primary outcome was in-hospital mortality, and we use multivariable logistic regression to calculate the odds of in-hospital mortality with andexanet alfa versus 4-factor PCCs.

The thing to take off this first results slide is the magnitude of this endeavor. The andexanet alfa group was over 2,100 subjects and the 4-factor PCC group was over 2,200 subjects, making it the largest endeavor to date. The mean age was about 65. About 60% were male. About 40% were taking rivaroxaban with the remainder of 60% taking apixaban. The bottom panel reveals our attempt at looking at a time-to-treatment parameter. The bottom left panel shows the time from last anticoagulant dose to admission so less than 8 hours in about 40%, 8 to 18 in about 40%, and a smattering about 15 to 17% were treated greater than 18 hours after last anticoagulant dose. A door-to-needle time, about 2.3 to 2.5 hours; it was evenly weighted in both treatment groups. I

In studies such as this it's important to ascertain whether or not both treatment groups were evenly weighted with their characteristics. And on the left, you see hypertension, diabetes, heart failure, chronic kidney disease, prior stroke, peptic ulcer disease, and liver

disease were all evenly weighted between these two groups. We also tried to look at alteration of sensorium, DNR order, and systolic blood pressure as well, and these were also evenly weighted among treatment groups.

In terms of the results, we saw high dose use of andexanet alfa in about 31% of treated subjects. With respect to 4-factor PCCs, it was a single dose with a median dose of about 2,200 units. This represents a dose of about 25 units per kilogram which is the lower side of that dosing strategy. In terms of bleeding location, about 60% of the patients exhibited GI bleeds, with about 30% exhibiting ICHs, with a lower cohort having noncompressible but critical compartment bleeding about 10%.

In this forest plot, you see the top line results. Clinical factors associated higher bleeding of death include the bleed type, age, impaired mental status, DNR order, and comorbidities. I'll call your attention to the top of the panel, andexanet alfa versus 4-factor PCCs. The andexanet alfa treated group was the only one that showed a lower risk of mortality in this cohort. Regardless of the type of ICH, you see that ICHs were associated with higher mortality in this treatment group. Age, impaired mental status, DNR order, liver disease, chronic kidney disease, and heart failure were all associated with higher mortality.

Interestingly, our attempt at looking at door-to-treatment parameters on the bottom really didn't result in any meaningful discrimination. Again, the top line results using a multivariable logistic regression. The adjusted odds of in-hospital mortality were 50% lower when using andexanet alfa versus 4-factor PCCs, that was about 10.6 versus 6.0.

In conclusion, this trial represents the largest observational study to date providing data on andexanet alfa in clinical practice. The odds of in-hospital mortality was 50% lower in patients treated with andexanet alfa versus 4-factor PCCs when adjusted for risk factors of mortality. Other factors associated higher odds of death include ICH and critical compartment bleeds versus GI bleeds, increasing age, presence of liver disease, chronic kidney disease, or heart failure, impaired mental status, and a DNR order. Limitations obviously are the same as you would see with any retrospective chart review.

Thank you for your participation. My name is Gregory Fermann from the University of Cincinnati.

Announcer:
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