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Title: Clinical Assessment of Andexanet Alfa in Patients Presenting with Life-Threatening Bleeds: A Real World Case Series

Purpose: Andexanet alfa is a recombinant, inactivated, therapeutic protein that mimics native coagulation Factor Xa. It is indicated for the reversal of apixaban and rivaroxaban in patients with life-threatening or uncontrolled bleeding. Andexanet alfa primarily works by binding and sequestering Factor Xa inhibitors, rapidly neutralizing the anticoagulant effects and restoring the natural ability to form a clot. Our hospital recently added andexanet alfa to the formulary and created a treatment protocol for use. The purpose of this case series evaluation was to assess each case of andexanet alfa utilization at our hospital, evaluate efficacy and appropriateness of use, and report our patient outcomes.

Methods: All patients who received andexanet alfa between June 2019 and November 2019 were identified from our internal andexanet alfa utilization log and included in this case series evaluation. Patient medical records were reviewed and data collection included significant past medical and medication history, type of bleed (spontaneous or trauma-related), bleed location, hematoma volume when available, andexanet alfa dosing as either high or low dose, setting of administration, reported adverse drug reactions, compliance with our hospital-approved utilization protocol, relevant laboratory values, and associated imaging tests used to assess resolution or progression of the bleeding. Reported outcomes included achievement of hemostasis based on computerized tomography (CT) scans for hematoma volume with intracranial hemorrhage, development of thromboembolic events after andexanet alfa administration, time until reinitiating anticoagulant treatment in each patient, and 30-day mortality when available. The institutional review board at our hospital granted approval for this study.

Results: Five patients with significant comorbidities and life-threatening bleeds were identified and received andexanet alfa for the acute reversal of either apixaban or rivaroxaban. Four of the patients presented with an intracranial hemorrhage, while one presented with a spinal bleed. Four of these patients received the low dose of andexanet alfa, while one patient received the high dose. Four of five patients experienced favorable outcomes with no symptom or hematoma volume progression, and were subsequently discharged. Three of four patients with CT scans experienced excellent or good hemostasis. One patient experienced a severe trauma related intracranial hemorrhage, a slight but potentially significant delay in treatment with andexanet alfa, and expired during the hospital stay due to extensive and continued progression of the hemorrhage. All four surviving patients resumed
anticoagulation without experiencing a thromboembolic event within 30 days of receiving andexanet alfa. No adverse drug reactions were reported during the study. In all 5 cases, andexanet alfa utilization was deemed appropriate according to study investigators and protocol compliance.

**Conclusion:** The efficacy of andexanet alfa has yet to be extensively studied in comparative studies or real-world scenarios. In our case series evaluation, the use of andexanet alfa as a reversal agent for apixaban or rivaroxaban in patients with life-threatening bleeds resulted in positive outcomes in four of five patients. Further evaluation is warranted to assess the efficacy of andexanet alfa and report outcomes in the clinical setting.