Evaluation of andexanet alfa versus prothrombin complex concentrate, 4-factor, unactivated in the reversal of Novel Oral Anticoagulant Agents (NOACs)

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Background/Purpose: Oral anticoagulants are widely used for the treatment and prevention of thromboembolism, and the newest guidelines now recommend choosing a NOAC over warfarin for eligible patients in the management of atrial fibrillation. For many years, 4-factor prothrombin complex concentrate (PCC-4) was the standard of care for reversing bleeding associated with oral anticoagulants, however, andexanet alfa was recently approved for the reversal of anticoagulation with rivaroxaban or apixaban. While andexanet alfa may seem like the most appropriate option for reversing factor Xa inhibitors, some facilities continue to use PCC-4 as the sole reversal agent in their institution. This study aims to compare mortality rates and costs of using the standard of care PCC-4 versus andexanet alfa in patients taking NOACs who have experienced a bleed while on therapy.

Methodology: Eligible participants are those ≥ 18 years of age who were taking either apixaban or rivaroxaban and received either andexanet alfa or PCC-4. This observational, retrospective study looked at mortality rates as the primary endpoint. Secondary endpoints included mortality secondary to a GI bleed versus an intracranial hemorrhage, the cost of treatment to the hospital for each drug, and the percentage of patients on appropriate NOAC regimens according to the indication present.

Results: There were more deaths in the andexanet alfa group than there were in the PCC-4 group when used for reversing NOACs, although this was not a statistically significant difference between the groups. The secondary endpoints were mortality associated with gastrointestinal bleed versus intracranial hemorrhage in patients taking a NOAC who received andexanet alfa versus PCC-4, and the difference in mortality rates for administration of weight-based dosing of PCC-4 compared to fixed-dosing of PCC-4, neither of which were statistically different. Other secondary endpoints were percentage of patients on an appropriate regimen, which was a majority of patients, and the costs associated with each reversal agent, which was much greater in the andexanet alfa group.

Conclusions: This study showed that there were no significant differences in mortality rates between andexanet alfa and PCC-4 utilization in reversing major bleeds associated with NOACs. More studies are needed to determine if PCC-4 remains a viable alternative to andexanet alfa, and to establish its place in therapy.