Title: Direct Oral Anticoagulants vs Warfarin for Treatment of Heparin-Induced Thrombocytopenia

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Background: Heparin-induced thrombocytopenia (HIT) is a rare, prothrombotic, adverse drug reaction that develops secondary to heparin exposure. Warfarin was the standard oral treatment option until direct oral anticoagulants (DOACs) were incorporated into the 2018 American Society of Hematology HIT guidelines. However, DOACs were included as a conditional recommendation with very low certainty of evidence about effects. Data to support their use in treatment of HIT is limited to small observational studies. Despite this lack of evidence, DOACs have become an increasingly popular option in clinical practice for treatment of HIT.

Objective: To compare the safety of DOACs vs warfarin for the treatment of confirmed HIT in adult patients within the Atrium Health system

Methods: This was a retrospective chart review from January 2019 through August 2021 of adult patients admitted to an Atrium Health facility with a documented HIT diagnosis which was identified with a diagnosis code. Patients were included if they were ≥ 18 years old, had a confirmed HIT diagnosis, and received treatment for HIT with either a DOAC or warfarin. Patients who were pregnant, had a mechanical heart valve, ventricular assisted device, presenting with non-acute HIT, or did not receive an oral anticoagulant were excluded. Patient specific demographics, laboratory data including renal function and platelet count, and clinical data including the presence of HIT associated thrombi and 4T scores were obtained from the electronic medical record. The primary outcome was the incidence of a major bleed as defined by the International Society on Thrombosis and Haemostasis (ISTH) within 30 days following the initiation of a DOAC or warfarin. Secondary outcomes included the development of a new venous and/or arterial thromboembolism or progression of thrombus within 30 days following the initiation of a DOAC or warfarin, and the incidence of minor bleeding as defined by the ISTH within 30 days following the initiation of a DOAC or warfarin. Baseline characteristics and outcomes were analyzed with descriptive statistics.

Results: Of the 186 patients assessed for eligibility, 46 patients met the inclusion criteria. The most common reason for being excluded was due a non-acute HIT diagnosis (57%). Twenty-four (52%) patients received a DOAC, while twenty-two (48%) patients received warfarin. The primary outcome occurred in one (4.2%) patient in the DOAC group and one (4.5%) in the warfarin group. The development of a new clot or progression of an existing clot occurred in two (8.3%) patients who received DOACs, while there were no occurrences in those who received warfarin. The incidence of a minor bleed was present in 1 (4.2%) patient who received a DOAC, and two (9.1%) patients who received warfarin.

Conclusion: This is the first comparative study to evaluate DOACs vs warfarin for the treatment of HIT. Based on this study's cohort, DOACs have similar safety and efficacy profile when compared to warfarin for the treatment of HIT. Based on our study and prior literature, DOACs continue to be a reasonable option, though more robust evaluation may still be needed.