BACKGROUND:
Rivaroxaban is an ideal potential treatment for heparin-induced thrombocytopenia (HIT) because it is administered orally by fixed dosing, requires no routine coagulation monitoring and has been proven effective in the treatment of venous and arterial thromboembolism in other settings.

STUDY DESIGN:
Canadian multicenter single-arm prospective cohort study of consecutive adult patients with suspected or confirmed HIT.

OBJECTIVES:
To evaluate the efficacy and safety of rivaroxaban in patients with suspected or confirmed HIT at 30 days.

METHODS:
• Patients with suspected HIT (4Ts score ≥4) were treated with rivaroxaban 15 mg bid until the diagnosis was supported or refuted by a local HIT assay.
• Patients with HIT confirmed by the local assay received rivaroxaban 15 mg bid until platelet recovery (or until Day 21 if the patient had acute thrombosis at study entry [HITT]) then stepped down to rivaroxaban 20 mg once daily until Day 30.
• Central testing with the serotonin-release assay (SRA) was performed for all patients, but not in real-time at all centers.
• All patients were contacted at Day 30 to enquire about thrombotic and bleeding events.

“HIT positive” defined as 4Ts score ≥4 plus ≥50% serotonin-release (mean) at three reaction conditions (heparin 0.1 U/mL; heparin 0.3 U/mL; enoxaparin 0.1 U/mL), as well as inhibition (<20% release or >50% inhibition) at heparin 100 U/mL and in the presence of Fc receptor-blocking monoclonal antibody, and a positive in-house ELISA.

Outcome Measures:
• Primary outcome measure: incidence of new, symptomatic, objectively-confirmed, venous or arterial thromboembolism in the combined cohort of patients with suspected and confirmed HIT
• Secondary outcome measures included incidence of symptomatic thromboembolism while on treatment with rivaroxaban (combined cohort) and the following among patients with SRA-confirmed HIT while on study treatment: incidence of venous and arterial thromboembolism, major bleeding and time to platelet recovery.

RESULTS:
• 200 patient sample size based on feasibility and an anticipated thrombotic event rate in the combined cohort of 6.5% at 30 days (5% in HIT negative; 11% in HIT positive) on while on rivaroxaban.
• In prior local studies, 6% of patients with suspected HIT were confirmed by the SRA therefore 10 to 30 participants out of 200 were anticipated to be HIT positive.
• Patients provided informed consent and the study was approved by the REB at each institution; www.clinicaltrials.gov NCT01598168

RESULTS:
22 participants enrolled Jan 2013-Jun 2015; study was terminated early after the minimum number of HIT positives due to poor recruitment.
HIT positives: mean per cent serotonin-release, 95%; 6 had received no other non-heparin anticoagulant prior to study enrolment.

EXCLUSION CRITERIA:
• Mechanical heart valve, severe renal insufficiency (CrCl<30 ml/min), hepatic disease with coagulopathy, clinically significant active bleeding or lesions at increased risk of bleeding within the past 6 mos., ongoing requirement for strong CYP 3A4 and Pgp inhibitors or inducers, pregnancy/nursing or study enrolment within past 100 days.
• Treatment with non-heparin anticoagulants prior to study enrolment was an exclusion criteria.

Sample Size Calculation:
200 patient sample size based on feasibility and an anticipated thrombotic event rate in the combined cohort of 6.5% at 30 days (5% in HIT negative; 11% in HIT positive) on while on rivaroxaban.

RESULTS:
85 M 100 No 40 4 None
79 M 100 No 57 15 None
80 M 98 Bilateral leg thrombosis 54 4 Bilateral leg amputation Day 15
71 F 100 Bilateral adrenal hemorrhage 300 Not applicable None
87 M 83 PE 111 2 None
61 M 90 Upper limb phlebitis – associated DVT 28 29 Extension of DVT Day 7 – full recovery post-catheter removal
82 F 89 Bilateral adrenal hemorrhage 164 Not applicable None
74 F 93 Not applicable None
86 F 89 Ant.DVT/Ill DVT and PE 36 8 None
60 M 100 No 21 Riv held after 2 doses for increased LFTs Death (cancer)
185 F 100 No 78 3 None
65 M 99 No 52 28 None

Table 1: HIT Positive Patients

CONCLUSIONS:
Rivaroxaban appears to be effective for treatment of HIT, although a small sample size and lack of a comparator make it an attractive option for treatment of HIT.