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DIRECT ORAL ANTICOAGULANT AND ART USAGE IN PLWH: DATA FROM THE DC COHORT

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Background

- CHEST guidelines recommend direct oral anticoagulants (DOACs) as first-line agents over warfarin for deep vein thromboembolism (DVT) and pulmonary embolism (PE) treatment.
- FDA approved DOACs: dabigatran (2010), rivaroxaban (2011), apixaban (2012), edoxaban (2015), and betrixaban (2017)
- DOAC dosing varies based on several factors (indication, age, weight, renal function). There are no well established surrogate markers for monitoring.
- Among PLWH receiving ART, an additional challenge is drug interaction potential between DOACs and strong CYP3A4 and p-glycoprotein (P-gp) inhibitors.
- **Use of DOACs with ritonavir (RTV) or cobicistat (COBI):**
  - **Rivaroxaban not recommended**
  - **Apixaban dose reduction required**
  - **Dabigatran dose reduction or avoidance may be necessary depending on renal function**

Study Objectives

- To characterize evolving trends in oral anticoagulant use in the DC Cohort
- To assess prevalence of concomitant use of DOACs with RTV or COBI boosted ART in this population

Methods

- The DC Cohort is a clinic-based, longitudinal observational cohort of PLWH established in 2011.
- Adult participants were included if they were prescribed oral anticoagulants (warfarin or DOACs) from January 1, 2011 to March 31, 2017. Eleven outpatient sites were included in this analysis.
- Study assessments:
  - Each individual course of a medication was considered a unique event. Overlap between prescriptions for warfarin, DOACs, and RTV or COBI was assessed.
  - Data on bleeding events following the initiation of warfarin or a DOAC was collected. Individual bleeds were defined as new ICD-9 or ICD-10 codes, separated by at least 30 days.
- Data collection included:
  - Demographics, pertinent medical history, laboratory results, ICD-9 and ICD-10 diagnoses, anticoagulant prescription details, concomitant medications, and bleeding events
- Descriptive statistics were generated, bivariate analyses were completed, and yearly trend in oral anticoagulant prescriptions was assessed.

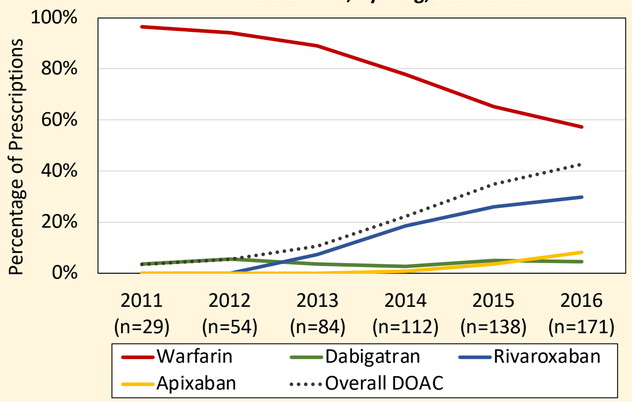
Results

- Among 8,315 PLWH, **236** anticoagulant prescriptions (96 DOAC, 140 warfarin) identified in 204 persons
- Anticoagulant indications included: non-pulmonary venous thromboembolism (26%), PE (20%), atrial fibrillation (11%)
- Most common ARTs were RAL or boosted DRV based

Table 1: Demographics and Baseline Characteristics

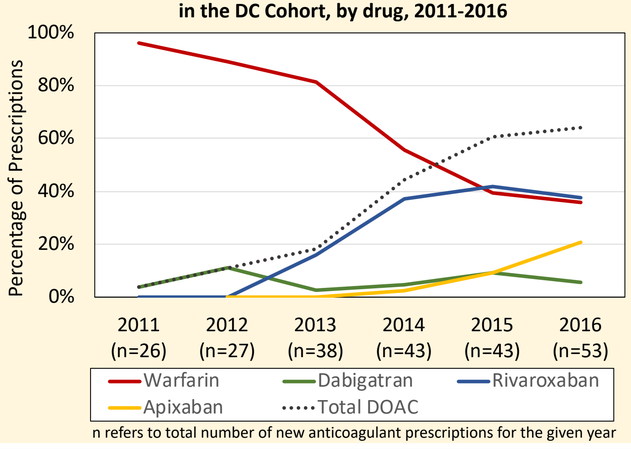
	DOAC (N=96)	Warfarin (N=140)	Overall (N=236)
Male (%)	84	80	82
Age at anticoagulation (years, mean ± SD)	58 ± 10.6	55 ± 11.1	56 ± 10.9
Black, n (%)	75 (78.1)	119 (85.0)	194 (82.2)
White, n (%)	13 (13.5)	13 (9.3)	26 (11.0)
Hispanic, n (%)	2 (2.1)	3 (2.1)	5 (2.1)
Weight, kg (mean ± SD)	84 ± 21 (n=74)	89 ± 29 (n=113)	87 ± 26 (n=187)
Comorbidities, n (%)			
Hypertension	50 (52.1)	67 (46.9)	117 (49.0)
CKD	33 (34.4)	54 (38.5)	87 (37.0)
Diabetes	24 (25.0)	35 (25.0)	59 (25.0)
Malignancy	22 (22.9)	32 (23.0)	54 (23.0)
Hepatic Impairment	13 (13.5)	19 (13.5)	32 (13.6)
HIV History			
ART at time of anticoagulation, n (%)	93 (97)	134 (96)	227 (96)
Time from HIV dx to anticoagulant start, (years, mean ± SD)	16 ± 9	15 ± 8	15 ± 8
CD4 prior to anticoagulant initiation (cells/mm³), n (%)			
<200	13 (14%)	15 (10%)	28 (10%)
200-500	30 (31%)	58 (41%)	88 (37%)
>500	42 (44%)	52 (37%)	94 (40%)
HIV-VL prior to anticoagulant initiation (c/ml), n (%)			
<200	72 (75%)	112 (80%)	184 (80%)
>200	12 (13%)	15 (11%)	27 (11%)

Figure 1: Trends in Overall Oral Anticoagulant Use in the DC Cohort, by drug, 2011-2016



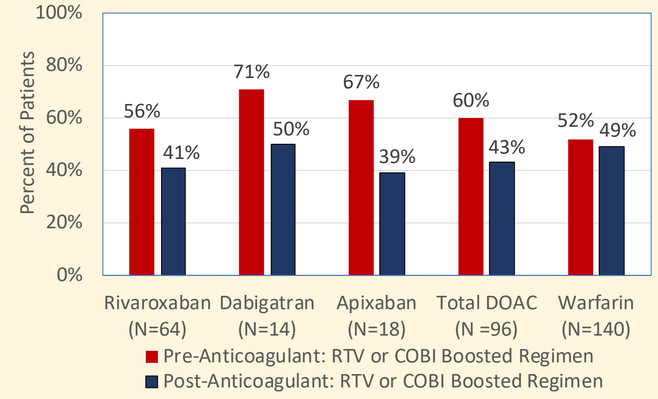
n refers to total number of patients on anticoagulation during the given year

Figure 2: New Oral Anticoagulant Starts in the DC Cohort, by drug, 2011-2016



n refers to total number of new anticoagulant prescriptions for the given year

Figure 3: Boosted ART Prescribing Patterns Pre- and Post- Initiation of Oral Anticoagulant



Changes in ART prescribing were assessed at 1 month post anticoagulation initiation. These changes were consistent at 6 months post anticoagulation.

- DOACs accounted for 3% of total anticoagulant use in 2011, increasing to 43% in 2016 (Figure 1). DOACs accounted for 64% of all new anticoagulant prescriptions by 2016 (Figure 2).
- 56% in the rivaroxaban group were receiving boosted ART prior to anticoagulant initiation. 41% still received boosted ART 1 month after rivaroxaban initiation, despite the recommendation to avoid concomitant use of combined P-gp and strong CYP3A4 inhibitors with rivaroxaban.
- 18 participants (7.6%) on ART and concomitant oral anticoagulation had a reported bleeding event, including 4.2% of DOAC patients and 12% of warfarin patients.
- No significant difference in the number of patients who had documented bleeds between those on boosted vs. un-boosted ART (p = 0.6621)

Conclusions

- DOAC use increased from 3% of all anticoagulant prescriptions in 2011 to 43% in 2016.
- Despite the recommendation to avoid co-administration with RTV or COBI boosted ART, concomitant use was documented in 41% of rivaroxaban recipients.
- Limitations of this analysis include: retrospective data collection with reliance on ICD 9 and 10 codes, DOAC dosing could not be fully evaluated (weight, renal function, other factors), and bleeding events were not systematically collected.
- Feedback should be provided to clinicians on DOAC utilization trends and potential ART drug interactions.

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