Bleeding and Procedure Rates Among Patients Treated With P2Y12 Inhibitors Compared with Factor Xa Inhibitors

A Real-World Analysis

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BACKGROUND

P2Y12 inhibitors (P2Y12i), Factor Xa inhibitors (FXai) and dabigatran (a direct thrombin inhibitor; DTi) are associated with increased risk of bleeding. Bleeding during surgery is a concern. Reversal agents exist for FXai and DTi. The present study examined bleeding events and rates of procedures in patients initiating these medications.

METHODS

The IBM MarketScan Commercial and Medicare Supplemental databases were utilized for the analyses. Patients newly initiating a P2Y12i, FXai inhibitor or DTi between 1/1/2014 to 6/30/2018 (earliest prescription = index date) were selected. All patients were required to present ≥1 year of baseline enrollment prior to index, and outcomes were measured while patients persisted on their index medication, defined as the time until a gap of ≥30 days or end of follow-up. Bleeding events were identified based on diagnosis codes on emergency room (ER) or inpatient claims. Procedures of interest were identified using the Healthcare Cost and Utilization Project procedure codes defined as 1) major and minor therapeutic, and 2) major diagnostic procedures. All procedures were classified as urgent (ER claims or inpatient claims with ambulance service) or non-urgent (all others). Patient clinical characteristics and demographics were assessed during the baseline period and on the index date respectively, while outcome measures were assessed during baseline and while persistent on index medication.

RESULTS

A total of 314,737 commercially insured and 202,068 Medicare supplemental patients qualified for the study. The distribution of drug indications in the 2 weeks preceding and inclusive of the index date are shown in Figures 1 and 2; baseline patient characteristics are presented in Table 1. P2Y12i patients in each payer group had a greater burden of several comorbidities than FXai and DTi patients (Table 1). Patients generally persisted with their index medication for ~1.2 years, with shorter persistence observed among Commercial patients (Figure 3). While persistent on their index medication, bleeding rates among P2Y12i patients were greater than bleeding rates among FXai and DTi patients (Figure 4). Rates of urgent and non-urgent procedures were generally similar or lower during the persistence period compared to baseline, with P2Y12i patients often presenting rates of these procedures greater than FXai and DTi patients (Figures 5 and 6).

CONCLUSION

Bleeding complications and medical procedures are common in patients taking antithrombotic medications. This study demonstrated that patients prescribed P2Y12i are at least equally as likely as patients using FXai and DTi to experience a bleeding event while persistent on their medication; in some populations, P2Y12i patients are potentially more likely to experience a bleed. Lower rates of urgent and non-urgent procedures in the persistence period, compared to baseline, may indicate delay of necessary procedures while taking these medications. While reversal agents exist for oral anticoagulants, no such agent exists for oral antiplatelets. As P2Y12i patients had bleeding rates and possible procedure delays at least as often as FXai and DTi patients, this study demonstrates an unmet need for an effective reversal agent for patients prescribed P2Y12i.

Currently, there is not an effective reversal agent for P2Y12 inhibitors.

In the present study, patients prescribed P2Y12 inhibitors presented bleeding rates, surgery rates and possible procedure delays that often exceeded rates observed among patients receiving FXa inhibitors and dabigatran, supporting the **need for an effective reversal agent for P2Y12 inhibitors**.

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FIGURE 1

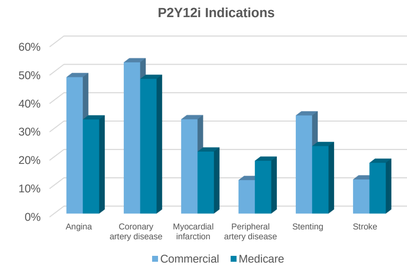


FIGURE 2

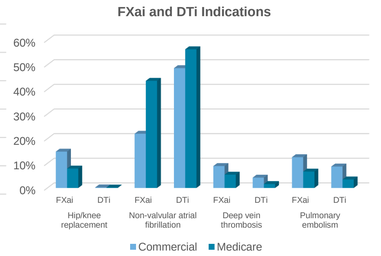


TABLE 1

	P2Y12i	FXai	DTi
Baseline Demographic/Clinical Characteristics			
Commercial	**N=132,715**	**N=175,996**	**N=6,026**
Age, Mean (SD)	55.4 (7.3)	53.2 (9.7)	54.7 (8.8)
Male	67.8%	53.8%	64.8%
Deyo Charlson Comorbidity Index, Mean (SD)	1.9 (1.9)	1.2 (2.0)	1.3 (1.9)
Cerebrovascular disease	23.5%	6.1%	9.6%
Chronic pulmonary disease	15.1%	15.9%	15.8%
Mild/moderate diabetes	32.8%	18.6%	22.1%
Diabetes with complications	10.7%	4.8%	5.5%
Renal disease	6.7%	4.4%	3.9%
Anemia	11.2%	16.9%	11.5%
Thrombocytopenia	2.0%	2.6%	2.5%
Medicare	**N=86,831**	**N=109,859**	**N=5,378**
Age, Mean (SD)	76.5 (7.8)	77.1 (7.7)	76.7 (7.5)
Male	57.1%	47.5%	54.0%
Deyo Charlson Comorbidity Index, Mean (SD)	3.1 (2.5)	2.4 (2.5)	2.2 (2.4)
Cerebrovascular disease	41.1%	19.0%	21.7%
Chronic pulmonary disease	25.1%	24.9%	23.9%
Mild/moderate diabetes	39.1%	28.4%	28.7%
Diabetes with complications	17.0%	10.9%	10.4%
Renal disease	18.6%	14.7%	12.0%
Anemia	23.1%	24.6%	19.1%
Thrombocytopenia	3.5%	3.9%	3.9%

FIGURE 3

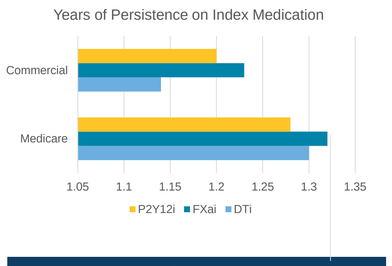


FIGURE 4

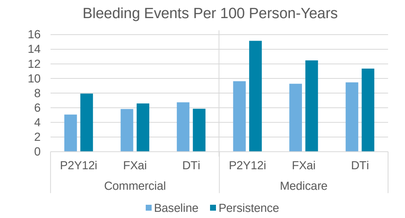


FIGURE 5

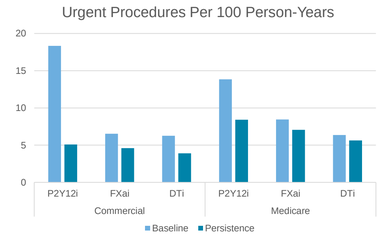
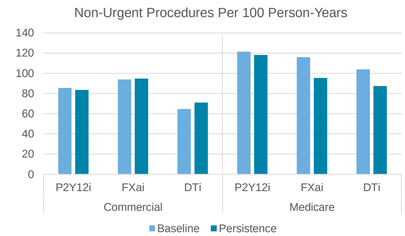


FIGURE 6



DISCLOSURE INFORMATION

Amanda Kong was employed at IBM Watson Health at the time of this analysis. Kristin Evans and Cynthia Morrow are current employees of IBM Watson Health. John Lee and Jeffrey Erickson are employees of PhaseBio Pharmaceuticals. Dr. Bhatt receives research funding paid to Brigham and Women's Hospital from PhaseBio and serves as the Chair of REVERSE-IT, studying the ticagrelor reversal agent bentracimab