PCR233

Adherence and Persistence of Oral Anticoagulants for Treatment of Atrial Fibrillation Across Stroke and Bleeding Risk Strata

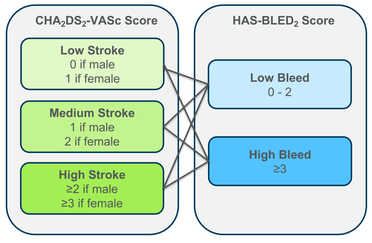
Gilbert Ko, PharmD, MBA, MS[1]; Elizabeth Brouwer, PhD, MPH[2]; Victoria Dayer, PharmD[2]; Arvind Katta, PharmD, MS[1]; Scott Ramsey, MD, PhD[2]; Rakesh Singh, PhD[1]; Sheldon Kong, PhD[1]; Maria Lopes, MD, MS[1]

[1]Bayer US LLC, Whippany, NJ, USA; [2]Curta, Inc., Seattle, WA, USA

Introduction

- Adherence and persistence rates differ among oral anticoagulants (OACs) in atrial fibrillation (AF) patients, and suboptimal adherence is associated with poor clinical outcomes.[1-3]
- Little evidence exists regarding treatment patterns, discontinuation, adherence, and persistence of OACs approved for stroke prevention among AF patients with different stroke and bleeding risks.
- Clinical outcomes vary in these risk groups; thus it is important to understand the differing treatment patterns and outcomes.

Figure 1. Stroke/Bleed Risk Subgroups



Objective

- This study aimed to evaluate variations in adherence and persistence to OACs among AF patients across stroke risk (CHA2DS2-VASc) and bleeding risk (HAS-BLED2) strata.

Methods

- Descriptive, retrospective cohort analysis
- National claims database: Optum
- Identified patients initiating an OAC between October 2016 – April 2021 (index date), with a diagnosis of AF during the baseline period (12 months prior to index), to assess adherence and persistence in the first year of treatment, based on index OAC. Follow-up period was defined as 12 months post index date.
- Inclusion criteria:
  - Age ≥45 years on index date
  - Continuous enrollment, ≥12 months pre-index and ≥12 months post-index
- Exclusion criteria:
  - Transient AF (pericarditis, hyperthyroidism, thyrotoxicity) during baseline period
  - Cardiac surgery during baseline period
  - Deep vein thrombosis, pulmonary embolism, or hip/knee replacement procedure within 6 months pre-index

Table 1. Study Definitions

Term	Definition
Discontinuation	• Discontinuation of index OAC (without re-initiation/switching) occurs when there is no re-initiation of index OACs or switch to another OAC from the last date of the last drug supply to the end of post-index follow-up period.
Re-initiation	• Therapy re-initiation occurs when there is re-initiation of index OAC more than 30 days after the last date of the last drug supply during the follow-up period.
Switching	• Therapy switching occurs when there is a switch from index OAC to another OAC.
Persistence	• Patients will be deemed persistent to OAC therapy until a prescription gap > 30 days on index OAC or an alternative OAC (switch) is reported. • Persistent days is the time period between index date and date of a prescription gap> 30 days on index OAC or an alternative OAC (switch) is reported.
Adherence	• Adherence is measured by Proportion of Days Covered (PDC) from the initiation of therapy to index OACs discontinuation, therapy re-initiation/switching or end of follow-up. • PDC is calculated as the number of days of medication supplied by the index OACs prescriptions divided by the length of therapy until discontinuation, re-initiation/switching or end of follow-up occurs.

Conclusions

- Adherence and persistence rates vary across stroke risk by drug, but generally decrease with increased bleeding risk within stroke risk groups.
- Newer therapies with lower bleeding risk are needed.

Results

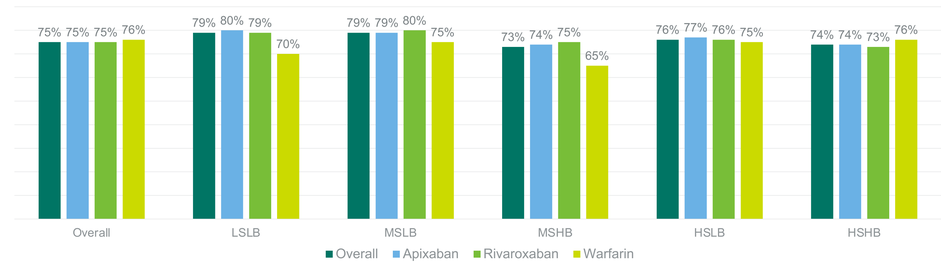
- Of 150,482 patients identified, the majority initiated with apixaban, rivaroxaban, and warfarin (66.9%, 20.4%, and 10.9% respectively, Table 2).
- **Persistence:**
  - Average overall persistence in the year after initiation was 228.3 days (SD 138.8).
  - Over 50% of patients were persistent at 6 months in all risk groups excepting low stroke and low bleed risk (37% for apixaban and rivaroxaban, 43% for warfarin) (Figure 2).
  - Persistence was highest for high stroke, low bleeding risk patients across all drugs (Figure 2).
- **Adherence:**
  - On average, 75.2% of the total population was adherent at least 80% of days covered with no significant difference between drugs (p=0.662) (Figure 3).
  - The highest percent of patients with PDC≥80% was 80% of patients using DOACs in low to medium stroke risk, regardless of bleed risk (Figure 3).
  - Adherence to apixaban and rivaroxaban decreased with increasing bleeding risk (Figure 3).
- **Discontinuation:** Overall, 21.3% of patients discontinued their index OAC (and did not re-initiate or switch)
- **Switching:** Most patients who switched from their index OAC switched to apixaban (Figure 4)

Figure 2. Persistence at 6 Months, by Index OAC and Risk Group

Abbreviations: High-Stroke, High-Bleed (HSHB); High-Stroke, Low-Bleed (HSLB); Low-Stroke, Low-Bleed (LSLB); Medium-Stroke, High-Bleed (MSHB); Medium-Stroke, Low-Bleed (MSLB)

Note: The Low-Stroke, High-Bleed group was omitted from this table due to low sample size (n=25)

Figure 3. Proportion of Patients with PDC ≥80%, by Index OAC and Risk Group



Abbreviations: Proportion of Days Covered (PDC); High-Stroke, High-Bleed (HSHB); High-Stroke, Low-Bleed (HSLB); Low-Stroke, Low-Bleed (LSLB); Medium-Stroke, High-Bleed (MSHB); Medium-Stroke, Low-Bleed (MSLB)

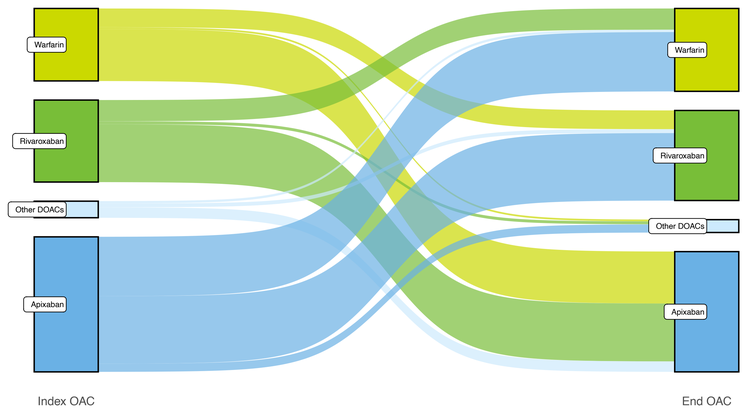
Note: The Low-Stroke, High-Bleed group was omitted from this table due to low sample size (n=25)

Table 2. Baseline Characteristics

	Overall	Apixaban	Rivaroxaban	Warfarin
Patient Population, N (%)	150,482	100,695 (66.9%)	30,653 (20.4%)	16,450 (10.9%)
Age, Mean (SD)	75.3 (9)	75.6 (8.9)	73.7 (9.4)	76.4 (8.4)
Age Group, N, (%)				
45-64 years	18,044 (12%)	11,213 (11.1%)	4,942 (16.1%)	1,400 (8.5%)
65-74 years	47,311 (31.4%)	31,077 (30.9%)	10,468 (34.2%)	4,868 (29.6%)
75-84 years	58,431 (38.8%)	39,292 (39%)	10,976 (35.8%)	7,216 (43.9%)
85+ years	26,696 (17.7%)	19,113 (19%)	4,267 (13.9%)	2,966 (18%)
Male, N (%)	79,521 (52.8%)	51,483 (51.1%)	17,490 (57.1%)	8,977 (54.6%)
Race, N (%)				
White	115,034 (76.4%)	76,758 (76.2%)	23,323 (76.1%)	12,861 (78.2%)
Black	13,276 (8.8%)	9,218 (9.2%)	2,561 (8.4%)	1,302 (7.9%)
Hispanic	13,017 (8.7%)	8,637 (8.6%)	2,822 (9.2%)	1,321 (8%)
Asian	3,377 (2.2%)	2,214 (2.2%)	764 (2.5%)	338 (2.1%)
Unknown	5,778 (3.8%)	3,868 (3.8%)	1,183 (3.9%)	628 (3.8%)
QCI Score, Mean (SD)	4.1 (2.9)	4.1 (2.9)	3.8 (2.8)	4.7 (3)
CHA2DS2-VASc Categorical Score, N (%)				
0 for Male or 1 for Female	2,691 (1.8%)	1,572 (1.6%)	900 (2.9%)	135 (0.8%)
1 for Male or 2 for Female	9,795 (6.5%)	6,150 (6.1%)	2,721 (8.9%)	652 (4%)
≥ 2 for Male or ≥ 3 for Female	137,992 (91.7%)	92,970 (92.3%)	27,031 (88.2%)	15,663 (95.2%)
HAS-BLED2 Categorical Score, N (%)				
0-2	80,201 (53.3%)	51,892 (51.5%)	18,064 (58.9%)	8,616 (52.4%)
≥ 3	70,281 (46.7%)	48,803 (48.5%)	12,589 (41.1%)	7,834 (47.6%)

Abbreviations: Atrial Fibrillation (AF); Not Applicable (NA); Oral anticoagulants(OAC); Quan-Charlson Index (QCI); Standard Deviation (SD)

Figure 4. Switching from Index OAC



Abbreviations: Oral anticoagulants(OAC); Direct-Acting Oral Anticoagulants (DOACs)

Note: The "Other DOACs" category represents therapies edoxaban and dabigatran

Table 3. Switching from Index OAC

Therapy Switching From Index Drug	Index Warfarin N=2,495	Index Rivaroxaban N=2,822	Index Other DOACs N=571	Index Apixaban N=4,648
Switch to Warfarin, N (%)	N/A	730 (25.9%)	80 (14%)	2043 (44%)
Switch to Rivaroxaban, N (%)	645 (25.9%)	N/A	131 (22.9%)	2324 (50%)
Switch to Other DOACs, N (%)	61 (2.4%)	100 (3.5%)	N/A	280 (6%)
Switch to Apixaban, N (%)	1789 (71.7%)	1992 (70.6%)	359 (62.9%)	N/A

Abbreviations: Direct Oral Anticoagulant (DOAC); Not Applicable (NA)

Note: The "Other DOACs" category represents therapies edoxaban and dabigatran

References

1. Cools F, Johnson D, Camm AJ, et al; for the GARFIELD-AF Investigators. Risks associated with discontinuation of oral anticoagulation in newly diagnosed patients with atrial fibrillation: Results from the GARFIELD-AF Registry. *J Thromb Haemost.* 2021; 19: 2322–2334. https://doi.org/10.1111/jth.15415
2. Komen JJ, Heerdink ER, Klungel OH, et al: Long-term persistence and adherence with non-vitamin K oral anticoagulants in patients with atrial fibrillation and their associations with stroke risk. *Eur Heart J Cardiovasc Pharmacother* 2021; 7:172-180
3. Borne RT, O'Donnell C, Turakhia MP, Varosy PD, Jackevicius CA, Marzec LN, Masoudi FA, Hess PL, Maddox TM, Ho PM. Adherence and outcomes to direct oral anticoagulants among patients with atrial fibrillation: findings from the veterans health administration. BMC Cardiovasc Disord. 2017 Sep 2;17(1):236. doi: 10.1186/s12872-017-0671-6.
4. Salmasi S, Loewen PS, Tandun R, et al. Adherence to oral anticoagulants among patients with atrial fibrillation: a systematic review and meta-analysis of observational studies. BMJ Open 2020;10:e034778. doi:10.1136/ bmjopen-2019-034778

Disclosures

This study is sponsored by Bayer AG. The sponsor was involved in the study design and the writing of the report.