**Stroke and Major Bleeding when Switching from Warfarin to Apixaban in Patients with Advanced Chronic Kidney Disease and Prevalent Atrial Fibrillation**

Katherine G. Garlo, MD1, Thomas A. Mavrakanas, MD, MSc, FRCPC, FASN,11,2, Burdick, Elisabeth, MS3, Wei Wang, PhD4, David M. Charytan, MD, MSc5

1Department of Medicine, Renal Division, Brigham & Women’s Hospital, Boston, MA2Division of Nephrology, Department of Medicine, McGill University Health Centre, Montreal, QC, Canada, 3The Center for Patient Safety Research and Practice, Brigham & Women’s Hospital, Boston, MA, USA,4 Division of Sleep and Circadian Disorders, Departments of Medicine and Neurology, Brigham and Women's Hospital, 5Department of Medicine, Nephrology Division, New York University Grossman School of Medicine, NY, USA

**Supplemental** **Table 1.** **ICD-9 and ICD-10 primary outcome diagnostic codes**

|  |  |
| --- | --- |
| **Diagnosis** | **ICD Code** |
| **Stroke** |  |
| Ischemic stroke or transient ischemic attack | **ICD-9-CM:** 362.3x, 433.x1, 434.x1, 436  **ICD-10 CM**: H34.1, I63 |
| Systemic thromboembolism | **ICD-9-CM:** 434.1, 444.xx, 445.xx |
| Hemorrhagic stroke | **ICD-10 CM**: I74, I75 |
|  | **ICD-9-CM**: 430, 431, 432  **ICD-10 CM**: I60, I61, I62 |
| **Major Bleeding**   1. Resulting in death 2. In a critical site   Intracranial  Intraocular  Pericardial  Airway  Intra-articular  Retroperitoneal   1. Resulting in hospitalization   Gastrointestinal  bleeding | **DEATHFM**: 38, 39, 40, 41, 42, 43, 72  **ICD-9-CM**:430, 431, 432.x  **ICD-10 CM**: I60, I61, I62  **ICD-10 CM**: I60, I61, I62  **ICD-9-CM**:360.43, 362.43, 362.81, 363.61, 363.62, 363.72, 376.32, 377.42, 379.23  **ICD-10 CM**: H44.81, H35.73x, H35.6x, H31.30x, H31.31x, H31.41x, H05.23x, H43.1x, H47.02x  **ICD-9-CM**:423.0 //  **ICD-10 CM**:I31.2  **ICD-9-CM**:784.8, 786.30, 786.39 //  **ICD-10 CM**:R04.x(x)  **ICD-9-CM**:719.1x //  **ICD-10 CM**:M25.0x(x)  **ICD-9-CM**:568.81//  **ICD-10 CM**:K66.1  One of the following codes in the institutional inpatient files:  **ICD-9-CM**: 456.0, 456.20, 530.21, 530.7, 530.82, 531.0x, 531.2x, 531.4x, 531.5x, 531.6x, 532.0x, 532.2x, 532.4x, 532.6x, 533.0x, 533.2x, 533.4x, 533.6x, 534.0x, 534.2x, 534.4x, 534.6x, 535.x1, 537.83, 537.84, 578.x, 562.x2, 562.x3, 569.3, 569.85 |
| Urinary bleeding  Gynecological bleeding  Other bleeding | **ICD-10 CM**: I85.x1, K22.11, K22.6, K25.0, K25.2, K25.4, K25.6, K26.0, K26.2, K26.4, K26.6, K27.0, K27.2, K27.4, K27.6, K28.0, K28.2, K28.4, K28.6, K29.x1, K31.811, K31.82, K92.0, K92.1, K92.2, K57.x1, K57.x3, K62.5, K55.21  **ICD-9-CM**: 596.7, 602.1, 599.7x  **ICD-10 CM**: N42.1, R31.0, R31.9  **ICD-9-CM**: 620.7, 621.4, 623.6, 624.5, 626.6, 626.8, 626.9, 627.0, 627.1  **ICD-10 CM**: N83.6, N83.7, N85.7, N92.0, N92.1, N92.4, N92.5, N93.8, N93.9, N95.0  **ICD-9-CM**: 459.0, 958.2, 729.92, 285.1 |

ICD = [International Statistical Classification of Diseases and Related Health Problems](https://en.wikipedia.org/wiki/International_Statistical_Classification_of_Diseases_and_Related_Health_Problems)

**Supplemental Table 2.** **Incidence of All Cause Stroke Composite Components in Patients with Prevalent Atrial Fibrillation on Warfarin who Switch to Apixaban versus Patients who Continue on Warfarin**

|  |  |  |
| --- | --- | --- |
| n (%) | **Warfarin Continue**  N=1691 | **Apixaban Switch**  N=71 |
| **Ischemic Stroke** | 250 (14.78) | <11 |
| **Systemic thromboembolism** | 29 (1.71) |  |
| **Hemorrhagic Stroke** | 22 (1.30) |  |
| **Transient Ischemic Attach** | <11 |  |

Individuals were censored at anticoagulation discontinuation, discontinuous Medicare part D, dialysis, kidney transplant, a 2nd switch in anticoagulant, or death. Poisson regression was used to estimate the incidence rates of the individual components of the stroke endpoint.

**Supplemental Table 3. Balance of Covariates using Inverse Probability of Treatment Weighting between Patients on Warfarin who Switch to Apixaban versus Patients who Continue on Warfarin**

|  |  |  |
| --- | --- | --- |
| Covariate | Standardized Difference **without** IPTW | Standardized Difference with IPTW |
| Age | -0.2301 | -0.1788 |
| CHA2DS2-VASc | -0.2884 | -0.1146 |
| HAS-BLED | -0.3726 | -0.2315 |
| Sex (male) | 0.1971 | -0.0768 |
| History of stroke | -0.2363 | -0.1045 |
| History of heart disease | -0.3468 | -0.0359 |
| History of major bleeding | -0.0288 | -0.0053 |
| History of diabetes mellitus | 0.0717 | 0.0012 |

Heart disease = myocardial infarction, coronary artery disease, or congestive heart failure; IPTW = inverse probability treatment weighting

**Supplemental Table 4.** **Adjusted Risk of Stroke and Major Bleeding in Patients with Atrial Fibrillation on Warfarin who Switch to Apixaban versus Continue on Warfarin Removing for Death within 90 Days of January 1, 2012 and Date of Apixaban Switch**

|  |  |  |
| --- | --- | --- |
|  | **Risk Estimate** | **P value** |
| **All Cause Stroke** |  |  |
| Adjusted HR (95% CI) | 0.33 (0.05-2.44) | 0.28 |
| **Major Bleeding** |  |  |
| Adjusted HR (95% CI) | 0.53 (0.07-3.85) | 0.53 |

Inverse probability treatment weighting (IPTW) adjusted survival analyses with death as competing risk were used to compare the time to first all cause stroke or major bleeding event between groups. The eight covariates used in the IPTW model were: age, sex, CHA 2DS2 -Vasc score, HAS-BLED score, history of stroke, history of bleeding, history of diabetes mellitus, history of heart disease (defined as either myocardial infarction, coronary artery disease, or congestive heart failure). Individuals were censored at anticoagulation discontinuation, discontinuous Medicare part D, dialysis, kidney transplant, a 2nd switch in anticoagulant, or death.

HR= hazard ratio; CI = confidence interval