**Supplementary Material**

**Supplementary table 1**: Number of patients and episodes analyzed.

|  |  |  |
| --- | --- | --- |
| Patients  n = 445 | DOAC per patient (n) | Episodes  n = 490 |
| 403  40  1  1 | 1  2  3  4 | 403   80   3  4 |

**Supplementary table 2**: Description of dose adjustments and crossover between DOACs.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Number switching** | **New DOAC prescribed** | |
| DOAC | no. |
| Total | 42/445 (9,4%) |  |  |
| Rivaroxaban | 16/165 (9.7%) |  |  |
| Rivaroxaban 20 mg | 12/87 (13,8%) | R15  A5  D110 | 7  4  1 |
| Rivaroxaban 15 mg | 4/78 (5,1%) | A2.5  A5  R20 | 2  1  1 |
| Dabigatran | 21/154 (13,6%) |  |  |
| Dabigatran 150 mg | 11/96 (11,4%) | A5  R20  D110 | 5  3  3 |
| Dabigatran 110 mg | 8/55 (14.5%) | A2.5  A5  D150  R15 | 4  2  1  1 |
| Dabigatran 75 mg | 2/3 (66,6%) | D110 | 2 |
| Apixaban | 5/126 (3.9%) |  |  |
| Apixaban 5 mg | 5/92 (5.4%) | A2.5  R15 | 4  1 |
| Apixaban 2.5 mg | 0/34 (0%) |  |  |

Only patients with the first dose adjustment or DOAC cross-over are shown.

(One patient switched 3 times: D150 => D110 => A5 => A2.5 and another patient switched twice: D75 => D110 => A2.5).

**Supplementary table 3**: Rate of appropriate dosing.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Apixaban | Dabigatran | Rivaroxaban | total |
| Appropriate dose | 122 (80.8%) | 135 (83.8) | 116 (65.2%) | 373 (76%) |
| Inappropriate dose  Low dose  High dose | 28 (18.5%)  1 (0.9%) | 24 (14.9%)  2 (1.2%) | 56 (31.4%)  6 (3.4%) | 108 (22%)  9 (1.8%) |

**Supplementary table 4**: Rates of thromboembolic events by study group

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Apixaban  2.5 mg  (n=46) | | Apixaban  5 mg  (n=105) | | Dabigatran  110 mg  (n=61) | | Dabigatran  150 mg  (n=97) | | Rivaroxaban  15 mg  (n=87) | | Rivaroxaban  20 mg  (n=91) | | Dabigatran  75 mg  *(n=3)* | | **Total**  **(n=490)** | |
|  | Patients  n | n/100  Pt-Yr | Patients  n | n/100  Pt-Yr | Patients  n | n/100  Pt-Yr | Patients  n | n/100  Pt-Yr | Patients  n | n/100  Pt-Yr | Patients  n | n/100  Pt-Yr | Patients  n | n/100  Pt-Yr | Patients  n | n/100  Pt-Yr |
| Total  - Stroke  - TIA | 1  0  1 | 1.26  0  1.26 | 4  3  1 | 2.07  1.55  0.52 | 4  4  0 | 3.67  3.67  0 | 2  2  0 | 1.13  1.13  0 | 8  6  2 | 4.6  3.45  1.15 | 0  0  0 | 0  0  0 | 1  0  1 | 24.14  0  24.14 | 20  15  5 | 2.18  1.64  0.54 |

Abbreviations: Pt-Yr = number of events per 100 patients-years of follow-up; TIA = transient ischemic attack.

Data are shown for treatment episodes with one or more events (one patient on rivaroxaban 15 mg suffered a TIA and subsequently a stroke).

No systemic thromboembolisms were observed.

**Supplementary table 5**: Rates of major and non-major clinically relevant (NMCR) bleeding events by study group.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Apixaban  2.5 mg  (n=46) | | Apixaban  5 mg  (n=105) | | Dabigatran  110 mg  (n=61) | | Dabigatran  150 mg  (n=97) | | Rivaroxaban  15 mg  (n=87) | | Rivaroxaban  20 mg  (n=91) | | Dabigatran  75 mg  *(n=3)* | | **Total**  **(n=490)** | |
| n | n/100  Pt-Yr | n | n/100  Pt-Yr | n | n/100  Pt-Yr | n | n/100  Pt-Yr | n | n/100  Pt-Yr | n | n/100  Pt-Yr | n | n/100  Pt-Yr | n | n/100  Pt-Yr |
| incidence rate of a first major and NMCR  bleeding event | | 2 | (2,5) | 11 | (5,7) | 10 | (9,2) | 13 | (7,4) | 9 | (5.2) | 12 | (6,6) | 0 | (0) | 57 | (6,2) |
| Incidence rate of any major and NMCR  bleeding eventa | | 5 | (6.3) | 12 | (6.2) | 11 | (10.1) | 15 | (8,5) | 9 | (5,2) | 16 | (8.7) | 0 | (0) | 68 | (7,4) |
| Major bleeding  NMCR bleeding | | 4  1 | (5)  (1.3) | 4  8 | (2.1)  (4.1) | 2  9 | (1.8)  (8.3) | 4  11 | (2.3)  (6.2) | 6  3 | (3.5)  (1.7) | 2  14 | (1.1)  (7.6) | 0  0 | (0)  (0) | 22  46 | **(2.4)**  **(5)** |
| Location | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Gastrointestinal | Total  Major  NMCR | 5\*  4  1 | (6.3)  (5)  (1.3) | 3  2  1 | (1.5)  (1.1)  (0.5) | 5  1  4 | (4.6)  (0.9)  (3.7) | 4  3  1 | (2.3)  (1.7)  (0.6) | 3  2  1 | (1.7)  (1.1)  (0.6) | 4  2  2 | (2.2)  (1.1)  (1.1) | *-*  *-*  *-* | *-*  *-*  *-* | 24  14  10 | (2.6)  (1.5)  (1.1) |
| Genitourinary | Total  Major  NMCR | -  -  - | -  -  - | 2\*  -  2 | (1.1)  -  (1.1) | 4  1  3 | (3.7)  (0.9)  (2.7) | 6\*  -  6 | (3.4)  -  (3.4) | 1  -  1 | (0.6)  -  (0.6) | 6\*  -  6 | (3.3)  -  (3.3) | *-*  *-*  *-* | *-*  *-*  *-* | 19  1  18 | (2.1)  (0.1)  (1.9) |
| Cranial | Total (all major) | - | - | 2\* | (1.1) | - | - | - | - | 3\* | (1.7) | - | - | *-* | *-* | 5 | (0.5) |
| Epistaxis | Total (all NMCR) | - | - | 3 | (1.5) | - | - | 1 | (0.6) | - | - | - | - | *-* | *-* | 4 | (0.4) |
| Hemoptysis | Total (all NMCR) | - | - | - | - | - | - | 1 | (0.6) | - | - | 3 | (1.6) | *-* | *-* | 4 | (0.4) |
| Muscular | Total (all NMCR) | - | - | - | - | 1 | (0.9) | - | - | 1 | (0.6) | - | - | *-* | *-* | 2 | (0.2) |
| Conjunctival | Total (all NMCR) | - | - | 1 | (0.5) | - | - | 1 | (0.6) | - | - | - | - | *-* | *-* | 2 | (0.2) |
| Gingivorrhagia | Total (all NMCR) | - | - | - | - | - | - | 1 | (0.6) | - | - | 1 | (0.5) | *-* | *-* | 2 | (0.2) |
| Ecchymosis | Total (all NMCR) | - | - | - | - | 1 | (0.9) | - | - | - | - | - | - | *-* | *-* | 1 | (0.1) |
| Other | Total (all NMCR) |  |  | 1 | (0.5) |  |  | 1 | (0.6) |  |  | 2 | (1.1) |  |  | 5 | (0.5) |

A dash (-) represents that there were no patients with events.

a. Several events, when they occur, are counted in the same episode within the period under study (5 patients each experienced 2 major/NMCR bleedings, 1 patient experienced 3 major/NMCR bleedings and 1 patient experienced 4 major/NMCR bleedings during the study period).

\* Includes patients with repeated events for episode in the same location due to an underlying bleeding pathology e.g. radiation proctitis and bladder, uterine or prostate cancer.

**Supplementary guide: Guide/Protocol for using DOACs developed at the Hospital.**

**Sagunto.san.gva.es/documents/7967159/7992985/guia\_nacos.pdf**