

SUPPLEMENTAL MATERIAL

Table S1. Interaction between internet participation and randomized dose with respect to outcomes (adherence and clinical).

| Outcome | CIF* Estimate at Median Follow-up (26.2 months) | | Incidence Rate (Events per 100 Patient Years of Follow-up) | | Unadjusted | | Adjusted‡ | |
|--|---|--------|--|--------------|-----------------------|---------|-----------------------|---------|
| | 81 mg | 325 mg | 81 mg | 325 mg | Hazard Ratio (95% CI) | P-value | Hazard Ratio (95% CI) | P-value |
| Medication Adherence | | | | | | 0.014 | | 0.019 |
| Endpoint: dose switching or aspirin discontinuation | | | | | | | | |
| Internet Participant | 18.58% | 55.42% | 10.79 (1053) | 41.89 (3118) | 0.28 (0.26 - 0.30) | | 0.28 (0.26 - 0.30) | |
| Non-internet Participant | 24.96% | 73.08% | 14.33 (193) | 77.89 (595) | 0.23 (0.19 - 0.27) | | 0.23 (0.19 - 0.27) | |
| Composite Clinical | | | | | | 0.150 | | 0.108 |
| Endpoint: all-cause death, myocardial infarction, or stroke | | | | | | | | |
| Internet Participant | 6.28% | 6.70% | 3.09 (439) | 3.19 (449) | 0.97 (0.85 - 1.10) | | 0.97 (0.85 - 1.11) | |
| Non-internet Participant | 13.73% | 12.96% | 7.29 (151) | 6.16 (120) | 1.18 (0.93 - 1.50) | | 1.22 (0.96 - 1.55) | |
| Safety Endpoint: Major bleeding with associated blood product transfusion | | | | | | 0.477 | | 0.440 |
| Internet Participant | 0.60% | 0.57% | 0.28 (41) | 0.26 (37) | 1.10** (0.70 - 1.71) | | 1.11 (0.71 - 1.75) | |
| Non-internet Participant | 0.80% | 0.76% | 0.56 (12) | 0.35 (7) | 1.60† (0.63 - 4.05) | | 1.67 (0.66 - 4.23) | |

*CIF: Cumulative Incidence Function

†Sub-distribution hazard ratio (SHR)

‡Models adjusted for age, sex, race, ethnicity and invitation method.

Table S2. Baseline characteristics and trial details of participants by internet participation at randomization and last observed visit.

| Characteristic | Overall (N=15,076) | Internet Participation at Randomization | | Non-Internet Participation at Randomization | |
|-------------------------------------|-----------------------|--|---|--|---|
| | | Internet Participant- Last Visit (N=11,474) | Non-internet Participant- Last Visit (N=1,698) | Internet Participant- Last Visit (N=13) | Non-internet Participant- Last Visit (N=1,891) |
| Age (yrs): median (IQR) | 68 (61 - 74) | 67 (60 - 73) | 68 (61 - 74) | 62 (56 - 67) | 69 (63 - 76) |
| Female | 4724 (31.3%) | 3428 (29.9%) | 556 (32.7%) | 5 (38.5%) | 735 (38.9%) |
| Race | | | | | |
| White | 11990 (79.5%) | 9695 (84.5%) | 1250 (73.6%) | 9 (69.2%) | 1036 (54.8%) |
| Black or African American | 1311 (8.7%) | 600 (5.2%) | 191 (11.2%) | 3 (23.1%) | 517 (27.3%) |
| Asian | 146 (1.0%) | 107 (0.9%) | 13 (0.8%) | 0 (0.0%) | 26 (1.4%) |
| American Indian or Alaska native | 114 (0.8%) | 74 (0.6%) | 14 (0.8%) | 0 (0.0%) | 26 (1.4%) |
| Multiple | 134 (0.9%) | 101 (0.9%) | 15 (0.9%) | 1 (7.7%) | 17 (0.9%) |
| Other | 401 (2.7%) | 168 (1.5%) | 34 (2.0%) | 0 (0.0%) | 199 (10.5%) |
| Not reported | 980 (6.5%) | 729 (6.4%) | 181 (10.7%) | 0 (0.0%) | 70 (3.7%) |
| Hispanic | 481 (3.2%) | 224 (2.0%) | 45 (2.7%) | 0 (0.0%) | 212 (11.2%) |
| Smoking Status | | | | | |
| Current | 1382 (9.8%) | 870 (8.2%) | 223 (13.4%) | 3 (23.1%) | 286 (15.2%) |
| Body Mass Index: median (IQR) | 30 (27 - 34) | 30 (27 - 34) | 30 (27 - 35) | 32 (29 - 36) | 30 (26 - 34) |
| Trial Details | | | | | |
| Randomized Dose | | | | | |
| 81 mg | 7540 (50.0%) | 5720 (49.9%) | 840 (49.5%) | 5 (38.5%) | 975 (51.6%) |

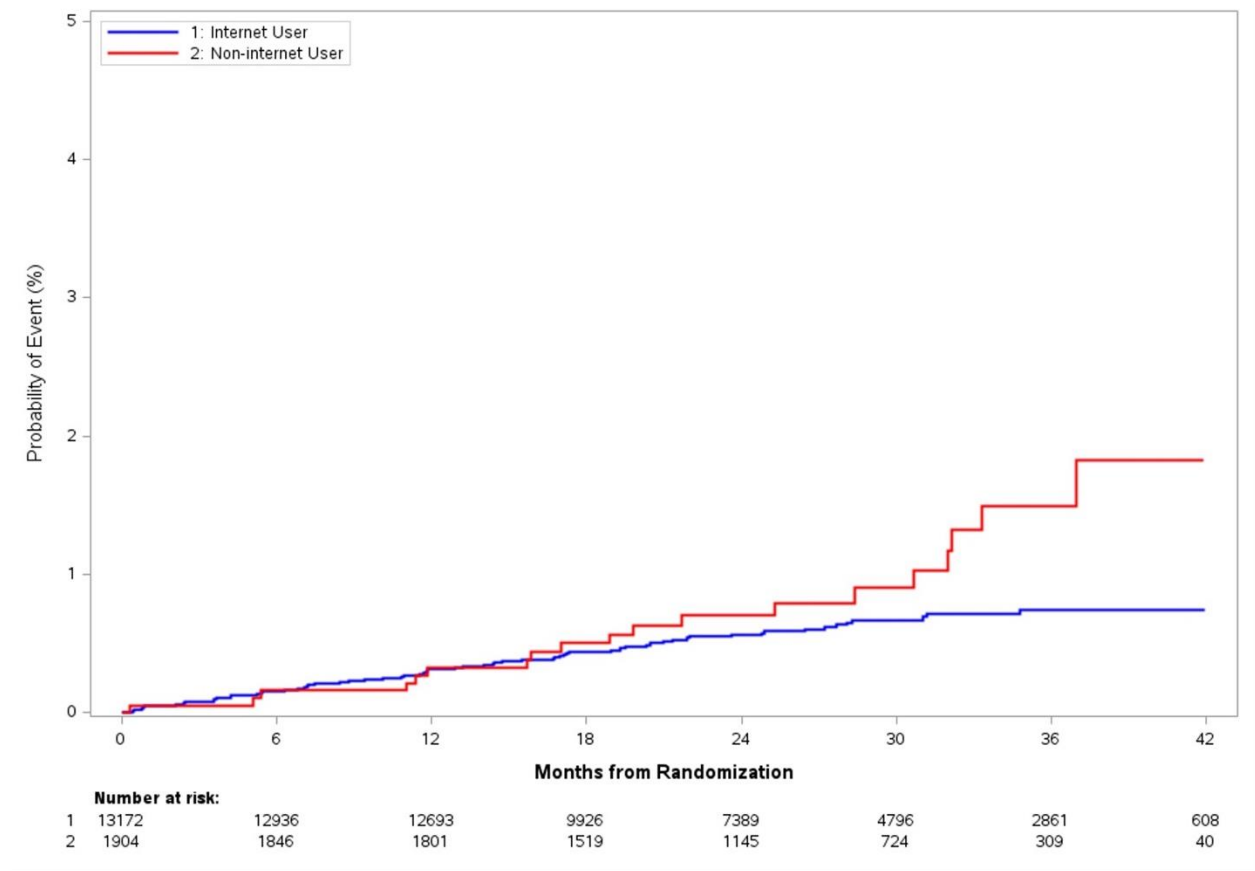
| | | | | | |
|---|---------------|--------------|--------------|------------|--------------|
| 325 mg | 7536 (50.0%) | 5754 (50.1%) | 858 (50.5%) | 8 (61.5%) | 916 (48.4%) |
| Randomized Follow-up Interval | | | | | |
| 3 Months | 7541 (50.0%) | 5775 (50.3%) | 829 (48.8%) | 7 (53.8%) | 930 (49.2%) |
| 6 Months | 7535 (50.0%) | 5699 (49.7%) | 869 (51.2%) | 6 (46.2%) | 961 (50.8%) |
| Invitation Method | | | | | |
| Received an Email | 5900 (39.1%) | 5344 (46.6%) | 503 (29.6%) | 2 (15.4%) | 51 (2.7%) |
| Received a Letter | 3400 (22.6%) | 2741 (23.9%) | 352 (20.7%) | 1 (7.7%) | 306 (16.2%) |
| Approached face-to-face in a clinical setting | 4080 (27.1%) | 2113 (18.4%) | 574 (33.8%) | 9 (69.2%) | 1384 (73.2%) |
| Contacted by Telephone | 1695 (11.2%) | 1275 (11.1%) | 269 (15.8%) | 1 (7.7%) | 150 (7.9%) |
| Medical History | | | | | |
| Prior Myocardial Infarction | 5305 (36.2%) | 3768 (33.9%) | 648 (39.0%) | 8 (61.5%) | 881 (46.7%) |
| Prior CABG* | 3527 (24.1%) | 2548 (23.0%) | 432 (26.0%) | 2 (15.4%) | 545 (28.9%) |
| Prior PCI† | 5946 (40.6%) | 4257 (38.3%) | 733 (44.2%) | 7 (53.8%) | 949 (50.3%) |
| Cerebrovascular Disease | 2624 (17.9%) | 1829 (16.5%) | 321 (19.3%) | 4 (30.8%) | 470 (24.9%) |
| Hypertension | 12512 (85.3%) | 9303 (83.8%) | 1448 (87.2%) | 12 (92.3%) | 1749 (92.7%) |
| Hyperlipidemia | 12946 (88.3%) | 9748 (87.8%) | 1493 (89.9%) | 11 (84.6%) | 1694 (89.8%) |
| Atrial Fibrillation | 1233 (8.4%) | 924 (8.3%) | 147 (8.9%) | 0 (0.0%) | 162 (8.6%) |
| Congestive Heart Failure | 3504 (23.9%) | 2345 (21.1%) | 460 (27.7%) | 4 (30.8%) | 695 (36.8%) |
| Peripheral Artery Disease | 3493 (23.8%) | 2321 (20.9%) | 444 (26.7%) | 1 (7.7%) | 727 (38.5%) |
| Diabetes Mellitus | 5676 (38.7%) | 3977 (35.8%) | 720 (43.4%) | 5 (38.5%) | 974 (51.6%) |
| History of Bleeding | 1267 (8.6%) | 862 (7.8%) | 170 (10.2%) | 2 (15.4%) | 233 (12.3%) |
| Significant Gastrointestinal Bleed | 950 (6.5%) | 640 (5.8%) | 123 (7.4%) | 2 (15.4%) | 185 (9.8%) |
| Intracranial Hemorrhage | 208 (1.4%) | 142 (1.3%) | 28 (1.7%) | 0 (0.0%) | 38 (2.0%) |
| Prior Medications | | | | | |

| | | | | | |
|--|---------------|---------------|--------------|---------------|---------------|
| Prior Aspirin Use | 13537 (96.0%) | 10098 (95.7%) | 1578 (95.1%) | 11 (84.6%) | 1850 (98.6%) |
| Prior Dose | | | | | |
| 81 mg | 11547 (85.4%) | 8580 (85.1%) | 1343 (85.5%) | 11 (100.0%) | 1613 (87.3%) |
| 162 mg | 310 (2.3%) | 256 (2.5%) | 28 (1.8%) | 0 (0.0%) | 26 (1.4%) |
| 325 mg | 1657 (12.3%) | 1249 (12.4%) | 200 (12.7%) | 0 (0.0%) | 208 (11.3%) |
| P2Y12 Inhibitor | 3051 (22.1%) | 2187 (21.0%) | 386 (25.2%) | 1 (8.3%) | 477 (25.5%) |
| Trial Adherence | | | | | |
| Percentage of Visits Completed: median (IQR) | 88 (67 - 100) | 93 (67 - 100) | 75 (60 - 86) | 89 (83 - 100) | 89 (73 - 100) |
| Categories of Visit Completion | | | | | |
| 0% | 775 (5.1%) | 763 (6.7%) | 2 (0.1%) | 0 (0.0%) | 10 (0.5%) |
| 1-25% | 659 (4.4%) | 506 (4.4%) | 39 (2.3%) | 1 (7.7%) | 113 (6.0%) |
| 26-50% | 1428 (9.5%) | 1011 (8.8%) | 241 (14.2%) | 0 (0.0%) | 176 (9.3%) |
| 51-75% | 2589 (17.2%) | 1646 (14.3%) | 659 (38.8%) | 0 (0.0%) | 284 (15.0%) |
| 76-99% | 2779 (18.4%) | 1838 (16.0%) | 412 (24.3%) | 7 (53.8%) | 522 (27.6%) |
| 100% | 6842 (45.4%) | 5707 (49.8%) | 345 (20.3%) | 5 (38.5%) | 785 (41.5%) |
| Number of Visits Completed with Call Center Assistance | 2 (1 - 3) | 1 (1 - 2) | 3 (2 - 4) | 3 (2 - 3) | 4 (2 - 6) |

*CABG: coronary artery bypass graft

†PCI: percutaneous intervention

Figure S1. Safety Endpoint: Major Bleeding Requiring Hospitalization.



Cumulative incidence function (CIF) curve for major bleeding by internet participation at randomization. At the median time of follow-up in the study, non-internet participants had more major bleeding events, widening the gap until the end of the study.