

SUPPLEMENTARY MATERIAL

Table S1. Distribution of patients by country with information on baseline OAC

| Country | N | Patients on OAC (row %) |
|----------------|------|----------------------------|
| Japan | 2836 | 80.9 |
| United Kingdom | 2172 | 70.4 |
| Germany | 1364 | 81.9 |
| Russia | 1181 | 57.3 |
| Spain | 1152 | 78.5 |
| Ukraine | 1123 | 52.7 |
| China | 1035 | 29.1 |
| Italy | 1035 | 89.8 |
| Belgium | 998 | 86.3 |
| Poland | 986 | 84.6 |
| Czech Republic | 941 | 78.0 |
| France | 870 | 80.3 |
| Thailand | 865 | 55.8 |
| South Korea | 845 | 65.0 |
| Hungary | 768 | 84.8 |
| India | 739 | 35.1 |
| Chile | 592 | 88.0 |
| Sweden | 560 | 85.5 |
| Argentina | 551 | 58.4 |
| United States | 534 | 72.7 |
| Brazil | 507 | 57.2 |
| Netherlands | 481 | 95.0 |
| Mexico | 454 | 62.3 |

| | | |
|-----------------------------|-----|------|
| Canada | 408 | 67.9 |
| Egypt | 367 | 89.7 |
| Turkey | 363 | 69.2 |
| Australia | 352 | 70.2 |
| South Africa | 330 | 77.6 |
| United Arab Emirates | 284 | 60.9 |
| Denmark | 213 | 85.5 |
| Singapore | 176 | 65.9 |
| Austria | 164 | 79.9 |
| Finland | 119 | 88.2 |
| Norway | 114 | 88.6 |
| Switzerland | 72 | 93.1 |

Table S2. Baseline characteristics by treatment at baseline

| Baseline characteristics | Patients treated with OAC | | | Patients not treated with OAC |
|---|---------------------------|------------------------|------------------------|-------------------------------|
| | FXaI (N = 7694) | DTI (N = 2090) | VKA (N = 8605) | OAC (N = 7162) |
| Body mass index, median (Q1; Q3), kg/m² | 26.6 (23.7;30.4) | 27.3 (24.4;31.6) | 27.6 (24.4;31.6) | 26.4 (23.5;30.1) |
| Systolic blood pressure, median (Q1; Q3), mmHg | 134.0 (120.0;146.0) | 131.0 (120.0;148.0) | 134.0 (120.0;147.0) | 130.0 (120.0;145.0) |
| Diastolic blood pressure, median (Q1; Q3), mmHg | 80.0 (70.0;88.0) | 80.0 (70.0;90.0) | 80.0 (70.0;90.0) | 80.0 (70.0;88.0) |
| Pulse, median (Q1; Q3), bpm | 84.0 (70.0;106.0) | 85.0 (70.0;110.0) | 85.0 (72.0;104.0) | 83.0 (70.0;105.0) |
| Care setting specialty at diagnosis, n (%) | | | | |
| Internal medicine/Neurology/Geriatrics | 1483 (19.3) | 339 (16.2) | 1819 (21.1) | 1493 (20.8) |
| Cardiology | 5387 (70.0) | 1546 (74.0) | 5227 (60.7) | 4632 (64.7) |
| Primary care/general practice | 824 (10.7) | 205 (9.8) | 1559 (18.1) | 1037 (14.5) |
| Care setting location at diagnosis, n (%) | | | | |
| Hospital | 3610 (46.9) | 1197 (57.3) | 4880 (56.7) | 4588 (64.1) |
| Office/Anticoagulation clinic/Thrombosis centre | 3375 (43.9) | 700 (33.5) | 2711 (31.5) | 1795 (25.1) |
| Emergency room | 709 (9.2) | 193 (9.2) | 1014 (11.8) | 779 (10.9) |
| Heavy alcohol consumption, n (%) | 109 (1.7) | 33 (1.9) | 130 (1.8) | 126 (2.1) |
| Current smoker, n (%) | 595 (8.5) | 189 (9.8) | 681 (8.6) | 636 (9.7) |

Table S3. Unadjusted and adjusted¹ hazard ratios and corresponding 95% confidence intervals for selected outcomes at two years of follow-up by treatment at baseline

| Outcome | Treatment comparison | | | | | | | |
|-----------------------------------|----------------------|---------|-----------------------|---------|--------------------|---------|-----------------------|---------|
| | OAC vs No OAC (ref.) | | | | NOAC vs VKA (ref.) | | | |
| | Unadjusted | | Adjusted ¹ | | Unadjusted | | Adjusted ¹ | |
| | HR (95% CI) | p-value | HR (95% CI) | p-value | HR (95% CI) | p-value | HR (95% CI) | p-value |
| All-cause mortality | 0.74 (0.68-0.81) | <0.0001 | 0.82 (0.74-0.91) | 0.0002 | 0.74 (0.67-0.82) | <0.0001 | 0.79 (0.70-0.89) | 0.0001 |
| Non-haemorrhagic stroke/SE | 0.67 (0.56-0.81) | <0.0001 | 0.71 (0.57-0.88) | 0.0021 | 0.82 (0.65-1.03) | 0.0877 | 0.96 (0.73-1.25) | 0.7360 |
| Major bleeding | 1.51 (1.22-1.88) | 0.0002 | 1.46 (1.15-1.86) | 0.0022 | 0.70 (0.57-0.85) | 0.0003 | 0.77 (0.61-0.98) | 0.0363 |

¹Obtained using an overlap-weighted Cox model. Variables included in the weighting scheme are: country and cohort enrolment, sex, age, ethnicity, type of AF, care setting speciality and location, congestive heart failure, acute coronary syndromes, vascular disease, carotid occlusive disease, prior stroke/TIA/SE, prior bleeding, VTE, hypertension, hypercholesterolemia, diabetes, cirrhosis, moderate to severe CKD, dementia, hyperthyroidism, hypothyroidism, current smoking, heavy alcohol consumption, BMI, heart rate, systolic and diastolic blood pressure at diagnosis, and baseline antiplatelet use.

Table S4. Unadjusted and adjusted¹ hazard ratios and corresponding 95% confidence intervals for selected outcomes at two years of follow-up by treatment at baseline

| Outcome | Treatment comparison | | | | | | | |
|-----------------------------------|-----------------------|---------|-----------------------|---------|----------------------|---------|-----------------------|---------|
| | NOAC vs No OAC (ref.) | | | | VKA vs No OAC (ref.) | | | |
| | Unadjusted | | Adjusted ¹ | | Unadjusted | | Adjusted ¹ | |
| | HR (95% CI) | p-value | HR (95% CI) | p-value | HR (95% CI) | p-value | HR (95% CI) | p-value |
| All-cause mortality | 0.64 (0.58-0.71) | <0.0001 | 0.67 (0.59-0.77) | <0.0001 | 0.86 (0.78-0.95) | 0.0035 | 0.93 (0.82-1.04) | 0.2088 |
| Non-haemorrhagic stroke/SE | 0.61 (0.49-0.76) | <0.0001 | 0.65 (0.50-0.86) | 0.0020 | 0.75 (0.60-0.93) | 0.0084 | 0.75 (0.58-0.98) | 0.0315 |
| Major bleeding | 1.26 (0.99-1.61) | 0.0627 | 1.10 (0.82-1.47) | 0.5239 | 1.80 (1.43-2.28) | <0.0001 | 1.86 (1.42-2.44) | <0.0001 |

¹Obtained using an overlap-weighted Cox model. Variables included in the weighting scheme are: country and cohort enrolment, sex, age, ethnicity, type of AF, care setting speciality and location, congestive heart failure, acute coronary syndromes, vascular disease, carotid occlusive disease, prior stroke/TIA/SE, prior bleeding, VTE, hypertension, hypercholesterolemia, diabetes, cirrhosis, moderate to severe CKD, dementia, hyperthyroidism, hypothyroidism, current smoking, heavy alcohol consumption, BMI, heart rate, systolic and diastolic blood pressure at diagnosis, and baseline antiplatelet use.

Table S5. Unadjusted and adjusted¹ hazard ratios and corresponding 95% confidence intervals for selected outcomes at two years of follow-up by OAC treatment at baseline. The reference considered is the treatment reported as second

| Outcome | Unadjusted HR (95% CI) | Adjusted ¹ HR (95% CI) |
|-----------------------------------|---------------------------|--------------------------------------|
| Baseline treatment | | |
| All-cause mortality | | |
| DTI vs VKA | 0.68 (0.57-0.82) | 0.83 (0.71-0.98) |
| FXaI vs VKA | 0.76 (0.68-0.85) | 0.77 (0.65-0.92) |
| FXaI vs DTI | 1.11 (0.92-1.35) | 0.92 (0.80-1.06) |
| Non-haemorrhagic stroke/SE | | |
| DTI vs VKA | 0.90 (0.62-1.30) | 1.01 (0.74-1.39) |
| FXaI vs VKA | 0.80 (0.63-1.02) | 0.92 (0.67-1.27) |
| FXaI vs DTI | 0.89 (0.61-1.31) | 0.91 (0.58-1.44) |
| Major bleeding | | |
| DTI vs VKA | 0.53 (0.36-0.77) | 0.68 (0.47-0.98) |
| FXaI vs VKA | 0.75 (0.61-0.92) | 0.84 (0.63-1.12) |
| FXaI vs DTI | 1.42 (0.95-2.11) | 1.24 (0.90-1.73) |

¹Obtained using an overlap-weighted Cox model. Variables included in the weighting scheme are: country and cohort enrolment, sex, age, ethnicity, type of AF, care setting speciality and location, congestive heart failure, acute coronary syndromes, vascular disease, carotid occlusive disease, prior stroke/TIA/SE, prior bleeding, VTE, hypertension, hypercholesterolemia, diabetes, cirrhosis, moderate to severe CKD, dementia, hyperthyroidism, hypothyroidism, current smoking, heavy alcohol consumption, BMI, heart rate, systolic and diastolic blood pressure at diagnosis, and baseline antiplatelet use.

Figure S1. Propensity score comparing OAC vs no OAC

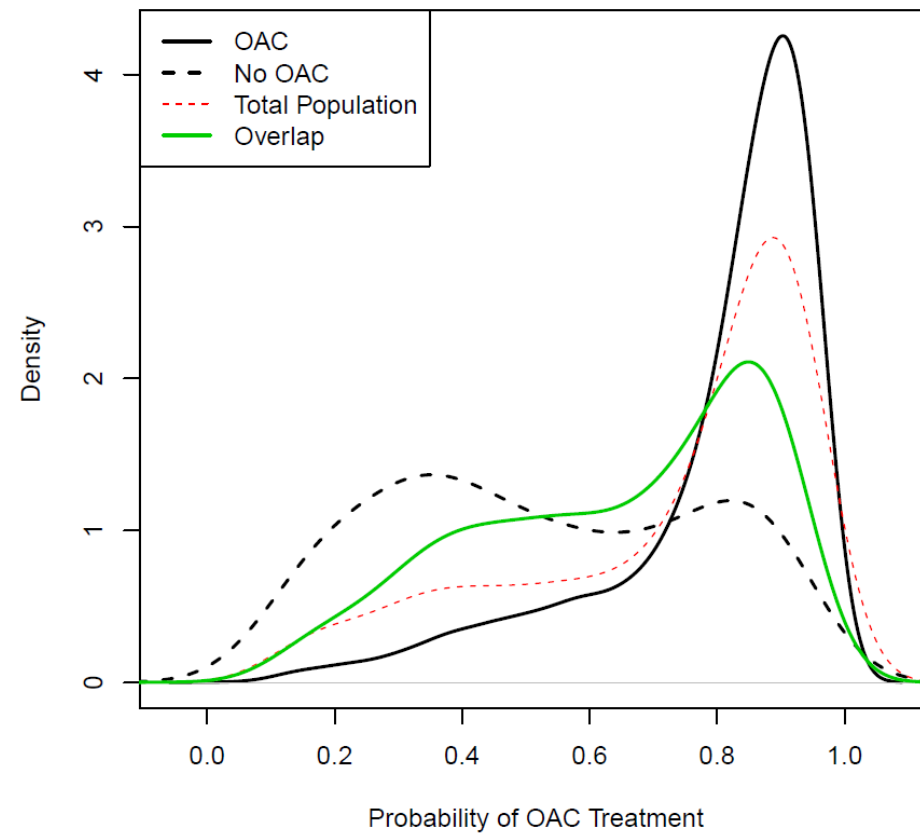


Figure S2. Propensity score comparing NOAC vs VKA

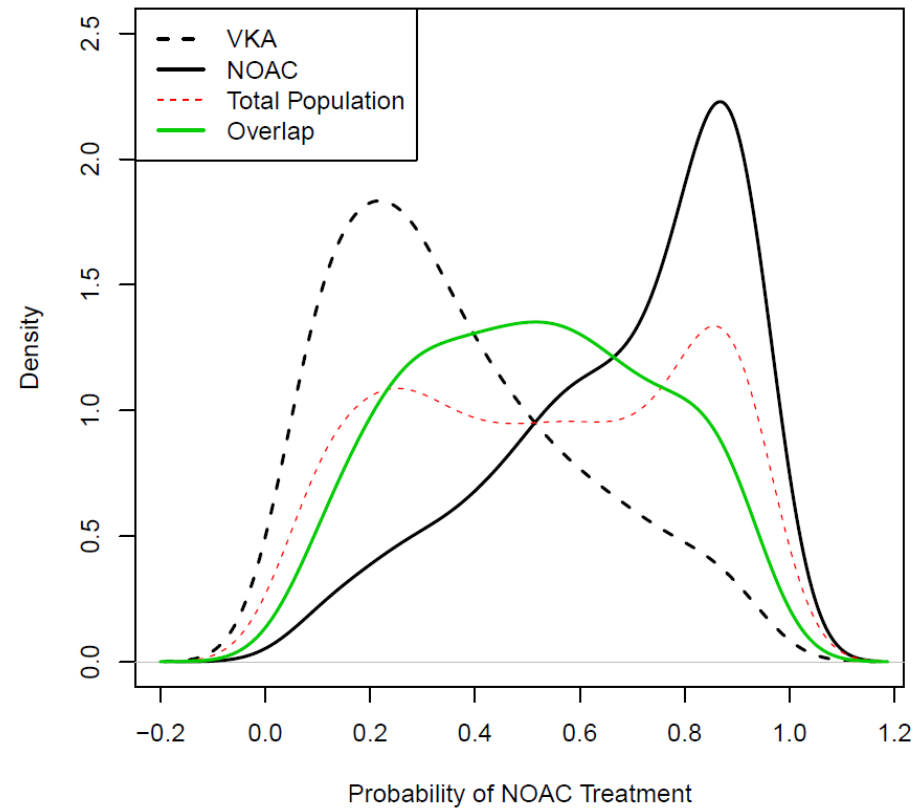


Figure S3. Balance of variables associated with OAC treatment in reference to no OAC treatment at baseline before and after propensity score weighting

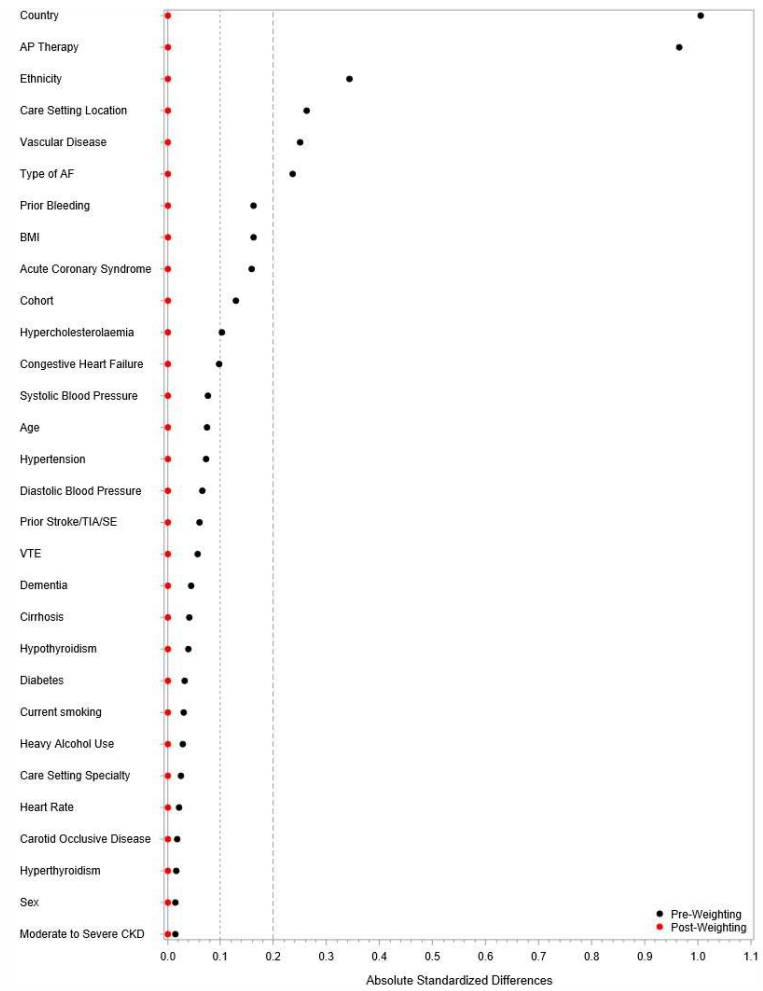


Figure S4. Balance of variables associated with NOAC treatment in reference to VKA treatment at baseline before and after propensity score weighting

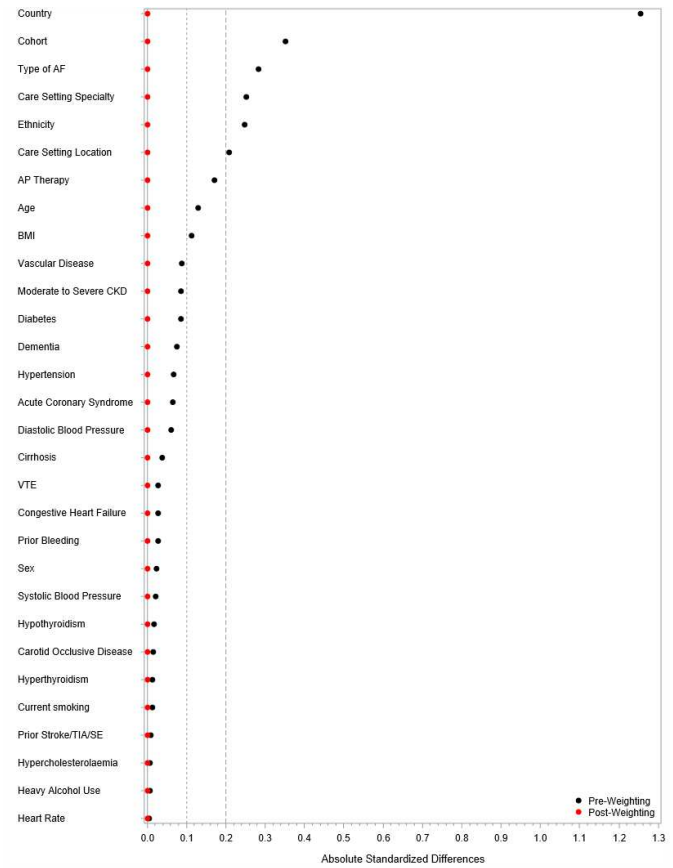


Figure S5. Flowchart for the selection of the study population

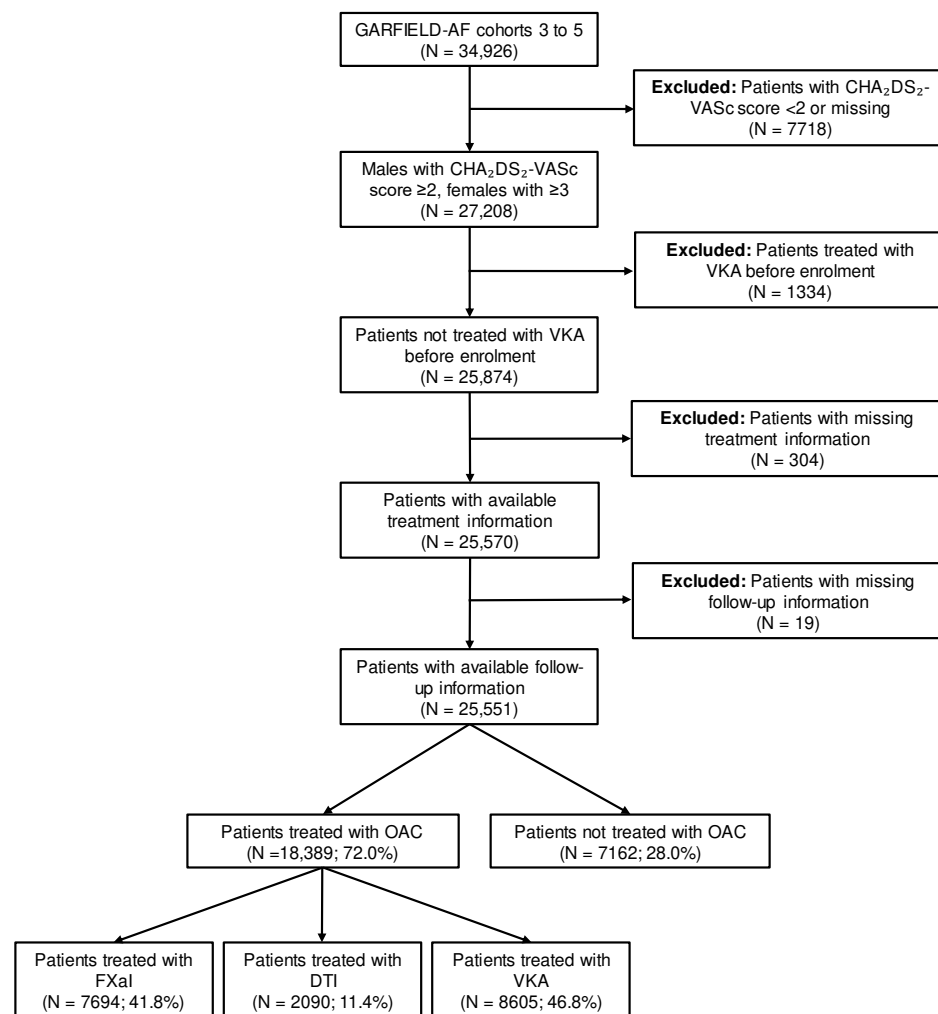
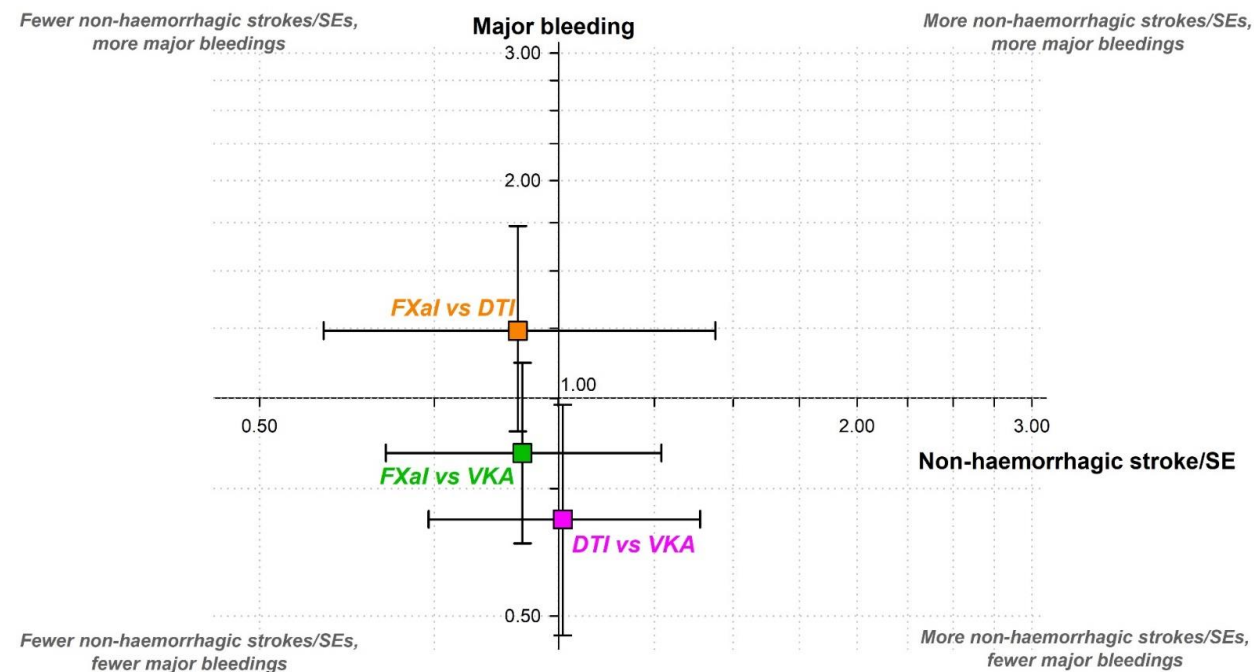


Figure S6. Adjusted¹ hazard ratios and corresponding 95% confidence intervals for selected outcomes at 2 years of follow-up by OAC treatment at baseline. The reference considered is the treatment reported as second



¹Obtained using an overlap-weighted Cox model. Variables included in the weighting scheme are: country and cohort enrolment, sex, age, ethnicity, type of AF, care setting speciality and location, congestive heart failure, acute coronary syndromes, vascular disease, carotid occlusive disease, prior stroke/TIA/SE, prior bleeding, VTE, hypertension, hypercholesterolemia, diabetes, cirrhosis, moderate to severe CKD, dementia, hyperthyroidism, hypothyroidism, current smoking, heavy alcohol consumption, BMI, heart rate, systolic and diastolic blood pressure at diagnosis, and baseline antiplatelet use.

GARFIELD-AF Registry Investigators

Global Steering Committee

Ajay K. Kakkar (UK) (Chair), Jean-Pierre Bassand (France), A. John Camm (UK), David A. Fitzmaurice (UK), Keith A.A. Fox (UK), Bernard J. Gersh (USA), Samuel Z. Goldhaber (USA), Shinya Goto (Japan), Sylvia Haas (Germany), Werner Hacke (Germany), Lorenzo G. Mantovani (Italy), Frank Misselwitz (Germany), Karen S. Pieper (USA), Alexander G.G. Turpie (Canada), Martin van Eickels (Germany), Freek W.A. Verheugt (the Netherlands).

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GARFIELD-AF National Investigators

China

Dayi Hu, Kangning Chen, Yusheng Zhao, Huaiqin Zhang, Jiyan Chen, Shiping Cao, Daowen Wang, Yuejin Yang, Weihua Li, Hui Li, Yuehui Yin, Guizhou Tao, Ping Yang, Yingmin Chen, Shenghu He, Yong Wang, Guosheng Fu, Xin Li, Tongguo Wu, Xiaoshu Cheng, Xiaowei Yan, Ruiping Zhao, Moshui Chen, Longgen Xiong, Ping Chen, Yang Jiao, Ying Guo, Li Xue, Zhiming Yang.

India

Praveen Jadhavm, Raghava Sarma, Govind Kulkarni, Prakash Chandwani, Rasesh Atulbhai Pothiwala, Mohanan Padinhare Purayil, Kamaldeep Chawla, Veerappa Annasaheb Kothiwale, Bagirath Raghuraman, Vinod Madan Vijan, Jitendra Sawhney, Ganapathi Bantwal, Aziz Khan, Ramdhan Meena, Manojkumar Chopada, Sunitha Abraham, Vikas Bisne, Govindan Vijayaraghavan, Debabrata Roy, Rajashekhar Durgaprasad, A.G. Ravi Shankar, Sunil Kumar, Dinesh Jain, Kartikeya Bhargava, Vinay Kumar, Udigala Madappa Nagamalesh, Rajeeve Kumar Rajput.

Japan

Yukihiro Koretsune, Seishu Kanamori, Kenichi Yamamoto, Koichiro Kumagai, Yosuke Katsuda, Keiki Yoshida, Fumitoshi Toyota, Yuji Mizuno, Ikuo Misumi, Hiroo Noguchi, Shinichi Ando, Tetsuro Suetsugu, Masahiro Minamoto, Hiroyuki Oda, Susumu Adachi, Kei Chiba, Hiroaki Norita, Makoto Tsuruta, Takeshi Koyanagi, Kunihiko Yamamoto, Hiroshi Ando, Takayuki Higashi, Megumi Okada, Shiro Azakami, Shinichiro Komaki, Kenshi Kumeda, Takashi Murayama, Jun Matsumura, Yurika Oba, Ryuji Sonoda, Kazuo Goto, Kotaro Minoda, Yoshikuni Haraguchi, Hisakazu Suefuji, Hiroo Miyagi, Hitoshi Kato, Tsugihiko Nakamura, Tadashi Nakamura, Hidekazu Nandate, Ryuji Zaitso, Yoshihisa Fujiura, Akira Yoshimura, Hiroyuki Numata, Jun Ogawa, Yasuyuki Kamogawa, Kinshiro Murakami, Yutaka Wakasa, Masanori Yamasawa, Hiromitsu Maekawa, Sumihisa Abe, Hajime Kihara, Satoru Tsunoda, Katsumi Saito, Hiroki Tachibana, Ichiro Oba, Takashi Kuwahata, Satoshi Higa, Masamichi Gushiken, Takuma Eto, Hidetoshi Chibana, Kazuaki Fujisawa, Yuhei Shiga, Hirokuni Sumi, Toshihisa Nagatomo, Yoshihiko Atsuchi, Toshiro Nagoshi, Kazuhisa Sanno, Fumihiro Hoshino, Naoto

Yokota, Masahiro Kameko, Toshifumi Tabuchi, Munesumi Ishizawa, Yoshitake Fujiura, Daisuke Ikeda, Taku Seto, Tetsu Iwao, Norio Ishioka, Koichi Oshiro, Keizo Tsuchida, Yutaka Hatori, Motoshi Takeuchi, Hiroto Takezawa, Shinjiro Nagano, Masaaki Iwaki, Yuichiro Nakamura, Naomasa Miyamoto, Toshifumi Taguchi, Ko Ashida, Naoto Yoshizawa, Jun Agata, Seishiro Matsukawa, Osamu Arasaki, Shuji Fukuoka, Hirofumi Murakami, Kazuya Mishima, Yoshiki Hata, Ichiro Sakuma, Kotaro Obunai, Ichiro Takamura, Mitsuyuki Akutsu, Toshihide Unoki, Yoshinori Go, Makoto Ikemura, Shoji Morii, Shigeru Marusaki, Hideo Doi, Mitsuru Tanaka, Takaaki Kusumoto, Shigeo Kakinoki, Chiga Ogurusu, Kazuya Murata, Masaki Shimoyama, Masami Nakatsuka, Yutaka Kitami, Yoichi Nakamura, Hiroshi Oda, Rikimaru Oyama, Masato Ageta, Teruaki Mita, Kazuhiko Nagao, Takafumi Mito, Junichi Minami, Mitsunori Abe, Masako Fujii, Makoto Okawa, Tsuneo Fujito, Toshiya Taniguchi, Tenei Ko, Hiroshi Kubo, Mizuho Imamaki, Masahiro Akiyama, Takashi Ueda, Hironori Odakura, Masahiko Inagaki, Yoshiki Katsube, Atsuyuki Nakata, Shinobu Tomimoto, Mitsuhiro Shibuya, Masayuki Nakano, Kenichiro Ito, Masahiro Matsuta, Motoyuki Ishiguro, Taro Minagawa, Masamichi Wada, Hiroaki Mukawa, Masato Mizuguchi, Fumio Okuda, Teruaki Kimura, Kuniaki Taga, Masaaki Techigawara, Morio Igarashi, Hiroshi Watanabe, Toshihiko Seo, Shinya Hiramitsu, Hiroaki Hosokawa, Mitsumoto Hoshiai, Michitaka Hibino, Koichi Miyagawa, Hideki Horie, Nobuyoshi Sugishita, Yukio Shiga, Akira Soma, Kazuo Neya, Tetsuro Yoshida, Kunio Akahane, Sen Adachi, Chiei Takanaka, Takashi Ueda, Saori Matsui, Hirofumi Kanda, Masanori Kaneko, Shiro Nagasaka, Atsushi Taguchi, Shuta Toru, Kazuyuki Saito, Akiko Miyashita, Hiroki Sasaguri, Jin Nariyama, Taketo Hatsuno, Takash Iwase, Kazuki Sato, Kazuya Kawai, Tomobumi Kotani, Tsuyoshi Tsuji, Hirosumi Sakai, Kiyoshi Nishino, Kenichi Ikeda, Kazuo Maeda, Tomohiro Shinozuka, Takeshi Inoue, Koichi Kawakami, Hiromichi Kitazumi, Tsutomu Takagi, Mamoru Hamaoka, Jisho Kojima, Akitoshi Sasaki, Yoshihiro Tsuchiya, Tetsuo Betsuyaku, Koji Higuchi, Masaaki Honda, Koichi Hasegawa, Takao Baba, Kazuaki Mineoi, Toshihiko Koeda, Kunihiko Hirasawa, Toshihide Kumazaki, Akira Nakagomi, Eiji Otaki, Takashi Shindo, Hiroyoshi Hirayama, Chikako Sugimoto, Takashi Yamagishi, Ichiro Mizuguchi, Kazunori Sezaki, Isamu Niwa, Ken Takenaka, Osamu Iiji, Koichi Taya, Hitoshi Kitazawa, samu Ueda, Hirokazu Kakuda, Takuya Ono, Seizo Oriso, Junya Kamata, Toshihiko Nanke, Itaru Maeda, Yoshifusa Matsuura, Hiroki Teragawa, Yasuyuki Maruyama, Kazuo Takei, Hajime Horie, Tetsutaro Kito, Hiroshi Asano, Koji Matsushita, Masaichi Nakamura, Takashi Washizuka, Tomoki Yoshida, Masato Sawano, Shinichi Arima, Hidekazu Arai, Hisanori Shinohara, Hiroyuki Takai, Nobufusa Furukawa, Akira Ota, Kentaro Yamamoto, Kenji Aoki, Taku Yamamoto, Takeaki Kasai, Shunji Suzuki, Shu Suzuki, Nitaro Shibata, Masayuki Watanabe, Yosuke Nishihata, Toru Arino, Masaki Okuyama, Tetsushi Wakiyama, Tomoko Kato, Yasuo Sasagawa, Takeshi Tana, Yoshihito Hayashi, Shinichi Hirota, Yukihiko Abe, Yoshihiro Saito, Hirohide Uchiyama, Hiroshi Takeda, Hiroshi Ono, Shuichi Tohyo, Naoto Hanazono, Seiichi Miyajima, Hisashi Shimono,

Takuma Aoyama, Yasunobu Shozawa, Yawara Nijima, Osamu Murai, Osamu Murai, Hideko Inaba, Katsumasa Nomura, Masatsugu Nozoe, Kazuo Suzuki, Toshiyuki Furukawa, Toshihiko Shiraiwa, Nobuhisa Ito, Shunichi Nagai, Kiyoharu Sato, Shiro Nakahara, Yujin Shimoyama, Naoko Ohara, Teruhiko Kozuka, Hideaki Okita, Masato Endo, Tsutomu Goto, Makoto Hirose, Emiko Nagata, Noriyuki Nakanishi, Toshizumi Mori, Shuichi Seki, Katsuhiro Okamoto, Osamu Moriai, Yoko Emura, Tsuyoshi Fukuda, Haruhiko Date, Shuichi Kawakami, Sho Nagai, Yuya Ueyama, Tetsuro Fudo, Mitsuru Imaizumi, Takuo Ogawa, Shunsuke Take, Hideo Ikeda, Hiroaki Nishioka, Norihiko Sakamoto, Kiyomitsu Ikeoka, Nobuo Wakaki, Masatake Abe, Junji Doiuchi, Tetsuya Kira, Masato Tada, Ken Tsuzaki, Naoya Miura, Yasuaki Fujisawa, Wataru Furumoto, Susumu Suzuki, Akinori Fujisawa, Ryosai Nakamura, Hiroyasu Komatsu, Rei Fujiki, Shuichi Kawano, Keijiro Nishizawa, Yoji Kato, Junya Azuma, Kiyoshi Yasui, Toshio Amano, Yasuhiro Sekine, Tatsuo Honzawa, Yuichiro Koshibu, Yasuhide Sakamoto, Yukihiro Seta, Shingo Miyaguchi, Kojuro Morishita, Yasuko Samejima, Toyoshi Sasaki, Fumiko Iseki, Toshiyuki Kobayashi, Hiroshi Kano, Jaeyoung Kim, Hiroshi Yamaguchi, Yoichi Takagi, Yoko Onuki Pearce, Yasuyuki Suzuki, Takayuki Fukui, Toru Nakayama, Hideaki Kanai, Yoshiyuki Kawano, Tetsuji Ino, Hironori Miyoshi, Yasufumi Miyamoto, Masahito Shigekiyo, Shimato Ono, Yoshiyuki Kawano, Yutaka Okamoto, Satoshi Ubukata, Kojiro Kodera, Tatsuo Oriuchi, Naoki Matsumoto, Koichi Inagaki, Atsushi Iseki, Tomohiro Yoshida, Toshihiro Goda, Tsukasa Katsuki, Atsushi Sato, Etsuo Mori, Toshio Tsubokura, Hiroshi Shudo, Shunichi Fujimoto, Tomohiro Katsuya, Yoshiyuki Furukawa, Hiroshi Hosokawa, Jun Narumi, Kiichiro Yamamoto, Masaki Owari, Takuya Inakura, Takafumi Anno, Kazuyuki Shirakawa.

Singapore

Chi Keong Ching, Toon Wei Lim, David Foo, Kelvin Wong, Tan Yuyang.

South Korea

Seil Oh, Hui Nam Park, Woo-Shik Kim, HyeYoung Lee, Sung-Won Jang, Dae Hyeok Kim, Jun Kim, DongRyeol Ryu, Jaemin Shim, Dae-Kyeong Kim, Dong Ju Choi, Yong Seog Oh, Myeong-Chan Cho, Hack-Lyoung Kim, Hui-Kyung Jeon, Dong-Gu Shin, Sang Weon Park, Hoon Ki Park, Sang-Jin Han, Jung Hoon Sung, Hyung-Wook Park, Gi-

Byoung Nam, Young Keun On, Hong Euy Lim, JaeJin Kwak, Tae-Joon Cha, Taek Jong Hong, Seong Hoon Park, Jung Han Yoon, Nam-Ho Kim, Kee-Sik Kim, Byung Chun Jung, Gyo-Seung Hwang, Chong-Jin Kim.

Thailand

Sakda Rungaramsin, Peerapat Katekangplu, Porames Khunrong, Thanita Bunyapipat, Wanwarang Wongcharoen, Pinij Kaewsuwanna, Khanchai Siri wattana, Waraporn Tiyanon, Supalerk Pattanaprichakul, Khanchit Likittanasombat, Doungrat Cholsaringkarl, Warangkana Boonyapisit, Sirichai Cheewatanakornkul, Songkwan Silaruks, Pisit Hutayanon, Seksan Chawanadelert, Pairoj Chattranukulchai, Boonsert Chatlaong, Yingsak Santanakorn, Khompiya Kanokphatcharakun, Piya Mongkolwongroj, Sasivimon Jai-Aue, Ongkarn Komson.

Turkey

Armagan Altun, Ali Aydinlar, Ramazan Topsakal, Zeki Ongen, Sadik Acikel, Durmus Yildiray Sahin, Ozcan Yilmaz, Mehmet Birhan Yilmaz, Hasan Pekdemir, Mesut Demir, Murat Sucu, Levent Sahiner, Ali Oto, Murat Ersanli, Ertugrul Okuyan, Dursun Aras.

Argentina

Florencia Rolandi, Adrian Cesar Ingaramo, Gustavo Alberto Sambadaro, Vanina Fernandez Caputi, Hector Luciardi, Sofia Graciela Berman, Pablo Dragotto, Andres Javier Kleiban, Nestor Centurion, Rodolfo Andres Ahuad Guerrero, Leonel Adalberto Di Paola, Ricardo Dario Dran, Javier Egido, Matias Jose Fosco, Victor Alfredo Sinisi, Luis Rodolfo Cartasegna, Oscar Gomez Vilamajo, Jose Luis Ramos, Sonia Sassone, Gerardo Zapata, Diego Conde, Guillermo Giacomi, Alberto Alfredo Fernandez, Mario Alberto Berli, Fabian Ferroni.

Brazil

Dário Celestino Sobral Filho, Jefferson Jaber, Luciana Vidal Armaganijan, Costantino Roberto Frack Costantini, André Steffens, Weimar Kunz Sebba Barroso de Souzaem, João David de Souza Neto, José Márcio Ribeiro, Marcelo Silveira Teixeira, Paulo Rossi, Leonardo Pires, Daniel Moreira, José Carlos Moura Jorge, Adalberto Menezes Lorga Filho, Luiz Bodanese, Marcelo Westerlund Montera, Carlos Henrique Del Carlo, Jamil Abdalla Saad, Fernando Augusto Alves da Costa, Renato Lopes, Gilson Roberto de Araújo, Euler Roberto Manenti, Jose Francisco Kerr Saraiva, João Carlos Ferreira Braga, Alexandre Negri, Carlos Moncada, Dalton Precoma, Fernando Roquette, Gilmar Reis, Roberto Álvaro Ramos Filho, Estêvão Lanna Figueiredo, Roberto Vieira Botelho, Cláudio Munhoz da Fontoura Tavares, Helius Carlos Finimundi, Adriano Kochi, César Cássio Broilo França, Fábio Alban, Guido Bernardo Aranha Rosito, João Batista de Moura Xavier Moraes Junior, Rogério Tadeu Tumelero, Lilia Maia, Roberto Simões de Almeida, Ney Carter do Carmo Borges, Luís Gustavo Gomes Ferreira.

Chile

Ramón Corbalán, Benjamin Aleck Joseh Stockins Fernandez, Humberto Montecinos, Fernando Lanás, Martín Larico Gómez, Carlos Astudillo, Carlos Conejeros, Patricio Marín Cuevas, Alejandro Forero, Claudio Bugeño Gutiérrez, Juan Aguilar, Sergio Potthoff Cardenas, German Eggert, Cesar Houzvic, Carlos Rey, Germán Arriagada, Gustavo Charme Vilches.

Mexico

Carlos Jerjes Sanchez Diaz, Jesus Jaime Illescas Diaz, Raul Leal Cantu, Maria Guadalupe Ramos Zavala, Ricardo Cabrera Jardines, Nilda Espinola Zavaleta, Enrique Lopez Rosas, Guillermo Antonio Llamas Esperón, Gerardo Pozas, Ernesto Cardona Muñoz, Norberto Matadamas Hernandez, Adolfo Leyva Rendon, Norberto Garcia Hernandez, Manuel de los Rios Ibarra, Luis Ramon Virgen Carrillo, David Lopez Villezca, Carlos Hernandez Herrera, Juan Jose Lopez Prieto, Rodolfo Gaona Rodriguez, Efrain Villeda Espinosa, David Flores Martinez, Jose Velasco Barcena, Omar Fierro Fierro, Ignacio Rodriguez Briones, Jose Luis Leiva Pons, Humberto Alvarez Lopez, Rafael Olvera Ruiz,

Carlos Gerardo Cantu Brito, Eduardo Julian Jose Roberto Chuquiure Valenzuela, Roxana Reyes Sanchez, Alberto Esteban Bazzoni Ruiz, Oscar Martin Lopez Ruiz, Roberto Arriaga Nava, Jesus David Morales Cerda, Pedro Fajardo Campos, Mario Benavides Gonzalez.

Austria

Marianne Brodmann, Kurt Lenz, Claus Hagn, Johannes Foechterle, Heinz Drexel, Kurt Huber, Andrea Podczeck-Schweighofer, Michael Winkler, Bruno Schneeweiss, Alfons Gegenhuber, Wilfried Lang, Sabine Eichinger-Hasenauer, Peter Kaserer, Josef Sykora, Heribert Rasch, Bernhard Strohmer.

Belgium

Luc Capiiau, Geert Vervoort, Bart Wollaert, Frank Cools, Geert Hollanders, Jan Vercammen, Dirk Faes, Yohan Balthazar, Marc Delforge, Olivier Xhaet, Harry Striekwold, John Thoeng, Kurt Hermans, Georges Mairesse, Wim Anné, Ivan Blankoff, Michel Beutels, Stefan Verstraete, Peter Vandergoten, Philippe Purnode, Pascal Godart, Tim Boussy, Philippe Desfontaines, Alex Heyse, Joeri Voet, Axel De Wolf.

Czech Republic

Eva Zidkova, Petr Jansky, Rudolf Spacek, Vilma Machova, Ondrej Ludka, Josef Olsr, Lubos Kotik, Blazej Racz, Richard Ferkl, Jan Hubac, Ilja Kotik, Zdenek Monhart, Hana Burianova, Ondrej Jerabek, Jana Pisova, Iveta Petrova, Vratislav Dedek, Michaela Honkova, Petr Podrazil, Petr Reichert, Jindrich Spinar, Miroslav Novak, Vaclav Durdil, Katarina Plocova, Jiri Lastuvka.

Denmark

Jørn Nielsen, Steen Husted, Helena Dominguez, Ulrik Hintze, Søren Rasmussen, Næstved Sygehus, Arne Bremmelgaard, John Markenvard, Jan Børger, Jorgen Solgaard, Ebbe Eriksen, Thomas Løkkegaard, Michael Bruun, Jacob Mertz, Morten Schou, Helena Dominguez, Michael Olsen.

Finland

Pekka Raatikainen, K.E. Juhani Airaksinen.

France

Franck Paganelli, Joël Ohayon, Frédéric Casassus, Jean-Yves Le Heuzey, Michel Galinier, Yannick Gottwalles, Philippe Loiselet, Jean-Joseph Muller, Mohamed Bassel Koujan, André Marquand, Sylvain Destrac, Olivier Piot, Nicolas Delarche, Jean-Pierre Cebron, Maxime Guenoun, Dominique Guedj-Meynier, Lokesh A G, Mathieu Zuber, Pierre Amarenco, Emmanuel Ellie, James Kadouch, Pierre-Yves Fournier, Jean-Pierre Huberman, Nestor Lemaire, Gilles Rodier, Xavier Vandamme, Igor Sibon, Jean-Philippe Neau, Marie Hélène Mahagne, Antoine Mielot, Marc Bonnefoy, Jean-Baptiste Churet, Vincent Navarre, Frederic Sellem, Gilles Monniot, Jean-Paul Boyes, Bernard Doucet, Michel Martelet, Désiré Obadia, Bernard Crousillat, Joseph Mouallem, Etienne Bearez, Jean Philippe Brugnaux, Alain Fedorowsky, Pierre Nazeyrollas, Jean-Baptiste Berneau, Frédéric Chemin.

Germany

Sebastien Schellong, Harald Darius, Georg Koeniger, Andreas Kopf, Uwe Gerbaulet, Bernd-Thomas Kellner, Thomas Schaefer, Jan Purr, Enno Eißfeller, Heinz-Dieter Zauzig, Peter Riegel, Christoph Axthelm, Gerd-Ulrich Heinz, Holger Menke, Andreas Pustelnik, Stefan Zutz, Wolfgang Eder, Guenter Rehling, Dirk Glatzel, Norbert Ludwig, Petra Sandow, Henning Wiswedel, Cosmas Wildenauer, Steffen Schoen, Toralf Schwarz, Adyeri Babyesiza, Maximilian Kropp, Hans-Hermann Zimny, Friedhelm Kahl, Andreas Caspar, Sabine Omankowsky, Torsten Laessig, Hermann-Josef Hartmann, Gunter Lehmann, Hans-Walter Bindig, Gunter Hergdt, Dietrich Reimer, Joachim Hauk, Holger Michel, Praxis Dres. Werner Erdle, Wilfried Dorsch, Janna Dshabrailov, Karl-Albrecht Rapp, Reinhold Vormann, Thomas Mueller, Peter Mayer, Uwe Horstmeier, Volker Eissing, Heinz Hey, Heinz Leuchtgens, Volker Lilienweiss, Heiner Mueller, Christian Schubert, Herrmann Lauer, Thomas Buchner, Gunter Brauer, Susanne Kamin, Karsten

Mueller, Sylvia Baumbach, Muwafeg Abdel-Qader, Hans-Holger Ebert, Carsten Schwencke, Peter Bernhardt, Laszlo Karolyi, Britta Sievers, Wilhelm Haverkamp, Jens-Uwe Roehnisch.

Hungary

Andras Vertes, Gabor Szantai, Andras Matoltsy, Nikosz Kanakaridisz, Zoltan Boda, Erno Kis, Balazs Gaszner, Ferenc Juhasz, Gizella Juhasz, Sandor Kancz, Zoltan Laszlo, Zsolt May, Bela Merkely, Ebrahim Noori, Tamas Habon, Peter Polgar, Gabriella Szalai, Sandor Vangel, Andras Nagy, Gabriella Engelthaler, Judit Ferenczi, Mihaly Egyutt.

Italy

Giuliana Martini, Leone Maria Cristina, Eros Tiraferri, Rita Santoro, Sophie Testa, Giovanni Di Minno, Marco Moia, Teresa Maria Caimi, Maria Tessitori, Giancarlo Agnelli, Roberto Cappelli, Daniela Poli, Roberto Quintavalla, Franco Cosmi, Raffaele Fanelli, Vincenzo Oriana, Raffaele Reggio, Roberto Santi, Leonardo Pancaldi, Raimondo De Cristofaro, Giuliana Guazzaloca, Angelo De Blasio, Jorge Salerno Uriate, Flavia Lillo, Enrico Maria Pogliani, Grzegorz Bilo, Michele Accogli, Antonio Mariani, Mauro Feola, Arturo Raisaro, Luciano Fattore, Andrea Mauric, Fabrizio Germini, Luca Tedeschi, Maria Settimi, Sergio Nicoli, Paolo Ricciarini, Antonio Argena, Paolo Ronchini, Claudio Bulla, Filippo Tradati, Massimo Volpe, Maria D'Avino, Maria Grazia Bongiorno, Silva Severi, Alessandro Capucci, Corrado Lodigiani, Enrico Salomone, Gaetano Serviddio, Claudio Tondo, Giuseppe Ambrosio, Paolo Golino, Carmine Mazzone, Saverio Iacopino.

The Netherlands

Hugo ten Cate, J.H. Ruiter, Andreas Lucassen, Henk Adriaansen, Maarten Bongaerts, Mathijs Pieterse, Coen van Guldener, Johannes Herrman, S.H.K. P.R. Nierop, Pieter Hoogslag, Walter Hermans, B.E. Groenemeijer, W. Terpstra, Cees Buiks, L.V.A. Boersma.

Norway

Eivind Berge, Per Anton Simes, Erik Gjertsen, Torstein Hole, Knut Erga, Arne Hallaråker, Gunnar Skjelvan, Anders Østrem, Beraki Ghezai, Arne Svilaas, Peter Christersson, Torbjørn Øien, Svein Høegh Henrichsen, Jan Erik Otterstad, Jan Berg-Johansen.

Poland

Janina Stepinska, Andrzej Gieroba, Malgorzata Biedrzycka, Michal Ogorek, Beata Wozakowska-Kaplon, Krystyna Loboż-Grudzien, Jaroslaw, Wieslaw Supinski, Jerzy Kuzniar, Roman Zaluska, Jaroslaw Hiczkiewicz, Lucyna Swiatkowska-Byczynska, Lech Kucharski, Marcin Gruchala, Piotr Minc, Maciej Olszewski, Grzegorz Kania, Malgorzata Krzciuk, Zbigniew Lajkowski, Bozenna Ostrowska-Pomian, Jerzy Lewczuk, Elzbieta Zinka, Agnieszka Karczmarczyk, Malgorzata Chmielnicka-Pruszczynska, Iwona Wozniak-Skowarska, Grzegorz Opolski, Marek Bronisz, Marcin Ogorek, Grazyna Glanowska, Piotr Ruszkowski, Grzegorz Skonieczny, Ryszard Sciborski, Boguslaw Okopien, Piotr Kukla, Krzysztof Galbas, Krzysztof Cymerman, Jaroslaw Jurowiecki, Pawel Miekus, Waldemar Myszka, Stanislaw Mazur, Roman Lysek, Jacek Baszak, Teresa Rusicka-Piekarz, Grzegorz Raczak, Ewa Domanska, Jadwiga Nessler, Jozef Lesnik.

Russia

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Spain

Xavier Vinolas, Pere Alvarez Garcia, Maria Fernanda Lopez Fernandez, Luis Tercedor Sanchez, Salvador Tranche Iparraguirre, Pere Toran Monserrat, Emilio Marquez Contreras, Jordi Isart Rafecas, Juan Motero Carrasco, Pablo Garcia Pavia, Casimiro Gomez Pajuelo, Luis Miguel Rincon Diaz, Luis Fernando Iglesias Alonso, Angel Grande Ruiz, Jordi Merce Klein, Jose Ramon Gonzalez Juanatey, Ines Monte Collado, Herminia Palacin Piquero, Carles Brotons Cuixart, Esther Fernandez Escobar, Joan Bayo i Llibre, Cecilia Corros Vicente, Manuel Vida Gutierrez, Francisco Epelde Gonzalo, Carlos Alexandre Almeida Fernandez, Encarnacion Martinez Navarro, Jordi Isart Rafecas, Juan Jose Montero Alia, Maria Barreda Gonzalez, Maria Angels Moleiro Oliva, Jose Iglesias Sanmartin, Mercedes Jimenez Gonzalez, Maria del Mar Rodriguez Alvarez, Juan Herreros Melenchon, Tomas Ripoll Vera, Manuel Jimenez Navarro, Maria Vazquez Caamano, Maria Fe Arcocha Torres, Gonzalo Marcos Gomez, Andres Iniguez Romo, Miguel Angel Prieto Diaz.

Sweden

Mårten Rosenqvist, Alexander Wirdby, Centrumkliniken, Jan Lindén, Kerstin Henriksson, Micael Elmersson, Arnor Egilsson, Ulf Börjesson, Gunnar Svärd, Bo Liu, Anders Lindh, Lars-Bertil Olsson, Mikael Gustavsson, Lars Andersson, Lars Benson, Claes Bothin, Ali Hajimirsadeghi, Björn Martinsson, Marianne Ericsson, Åke Ohlsson, Håkan Lindvall, Peter Svensson, Katarina Thörne, Hans Händel, Pyotr Platonov, Fredrik Bernsten, Ingar Timberg, Milita Crisby, Jan-Erik Karlsson, Agneta Andersson, Lennart Malmqvist, Johan Engdahl, Jörgen Thulin, Aida Hot-Bjelak, Steen Jensen, Per Stalby.

Switzerland

Jan Steffel, Johann Debrunner, Juerg H. Beer, Dipen Shah.

Ukraine

Iurii Rudyk, Vira Tseluyko, Oleksandr Karpenko, Svitlana Zhurba, Igor Kraiz, Oleksandr Parkhomenko, Iryna Kupnovytska, Nestor Seredyuk, Yuriy Mostovoy, Oleksiy Ushakov, Olena Koval, Igor Kovalskiy, Yevgeniya Svyschenko, Oleg Sychov, Mykola Stanislavchuk, Andriy Yagensky, Susanna Tykhonova, Ivan Fushtey.

United Kingdom

Will Murdoch, Naresh Chauhan, Daryl Goodwin, Louise Lumley, Ramila Patel, Philip Saunders, Bennett Wong, Alex Cameron, Philip Saunders, Niranjana Patel, P Jhittay, Andrew Ross, M S Kainth, Karim Ladha, Kevin Douglas, Gill Pickavance, Joanna McDonnell, Laura Handscombe, Trevor Gooding, Helga Wagner, Cumberlidge, Colin Bradshaw, Catherine Bromham, Kevin Jones, Shoeb Suryani, Richard Coates, Bhupinder Sarai, W Willcock, S Sircar, John Cairns, A Gilliland, Roman Bilas, E Strieder, Peter Hutchinson, Anne Wakeman, Michael Stokes, Graham Kirby, Bhaskhar Vishwanathan, Nigel Bird, Paul Evans, M Clark, John Bisatt, Jennifer Litchfield, E Fisher, Tim Fooks, Richard Kelsall, Neil Paul, Elizabeth Alborough, Michael Aziz, C Ramesh, Pete Wilson, Simon Franklin, Sue Fairhead, Julian Thompson, Hasan Chowan, Gary Taylor, Dawn Tragen, Matt Parfitt, Claire Seamark, Carolyn Paul, Mark Richardson, Angus Jefferies, Helen Sharp, Hywel Jones, Claire Giles, Matthew Bramley, Philip Williams, Jehad Aldegather, Simon Wetherell, William Lumb, Phil Evans, Frances Scouller, Neil Macey, Stephen Rogers, Yvette Stipp, Richard West, Philip Pinney, Paul Wadeson, John Matthews, Preeti Pandya, Andrew Gallagher, T Railton, Emyr Davies, Jonathan McClure, Marc Jacobs, Claire Hutton, R Thompson, Bijoy Sinha, Keith Butter, Susan Barrow, Helen Little, David Russell, Ulka Choudhary, Ikram Haq, Paul Ainsworth, Claire Jones, Phil Weeks, Jane Eden, Lisa Gibbons, Janet Glencross, Alison MacLeod, K Poland, Conor Mulolland, A Warke, Paul Conn, D Burns, R Smith, R Kamath, Jonathan Webster, Ian Hodgins, Stephen Vercoe, Paul Roome, Hilary Pinnock, Jayesh Patel, Amar Ali, Nigel Hart, Richard Davies, Nigel De-Sousa, Catherine Neden, Mark Danielsen, Purnima Sharma, Sophia Galloway, Charlotte Hawkins, Raife Oliver, Martin Aylward, Mira Pattni, Gordon Irvine, Shahid Ahmad, Catherine Rothwell, Fiaz Choudhary, Sabrina Khalaque, Stephanie Short, Sharon Peters, Warwick Coulson, Neil Roberts, Amy Butler, Steven Coates, Ben Ward, Daniel Jackson, Steve Walton, Diane Shepherd, Toh Wong, Mark Boon, Melanie Deacon, David Cornelius, Sarah Davies, Ben Frankel, Nick Hargreaves, Henry Choi, Jon Sumner, Tim Myhill, Salah Estifanos, Diane Geatch, Justin Wilkinson, Richard Veale, Karen Forshaw, Rob Hirst, Kashif Zaman, Catherine Liley,

Rebecca Wastling, Paul McEleny, Andre Beattie, Philip Cooke, Mike Wong, Mark Pugsley, Chaminda Dooldeniya, Greg Rogers, James Bennett, Polly Jacobs, Rajesh Muvva, Matthew Adam, Robin Fox, Nicolas Thomas, Simon Cartwright, Rory Reed, Simon Randfield, Christine A'Court, Ann Flynn, Andrew Halpin, Shoeb Suryani, Simon Dobson, Louise Lomax, Minnal Nadaph, Iain Munro, Jane Goram, Helen Stoddart, Phil Simmons, John Shewring, Emma Bowen-Simpkins, Mark Rickenbach, Polly Jacobs.

Australia

Adam Blenkhorn, Bhuwanendu Singh, Penny Astridge, William van Gaal, Walter Abhayaratna, Philip Thomson, Ron Lehman, Jens Kilian, David Coulshed, Andrei Catanchin, David Colquhoun, Hosen Kiat, David Eccleston, John French, Bronte Ayres, Peter Blombery, Thanh Phan, James Rogers, David O'Donnell, Sang Cheol Bae, Harry Gibbs, Patrick Carroll, Greg Starmer, Margaret Arstall, Maurits Binnekamp, Astin Lee.

Canada

John Eikelboom, Robert Luton, Milan Gupta, Amritanshu Shekhar Pandey, Stephen Cheung, Rolland Leader, Philippe Beaudry, Félix Ayala-Paredes, Joseph Berlingieri, John Heath, Germain Poirier, Miranda du Preez, Bradley Schweitzer, Reginald Nadeau, Ripple Dhillon, Tomasz Hruczkowski, Andrea Lavoie, Ratika Parkash, James Cha, Benoit Coutu, Paul MacDonald, Brian Ramjattan, Jorge Bonet, Saul Vizel, Paul Angaran, Sameh Fikry.

Egypt

Ahmed Mowafy, Azza Katta, Mazen Tawfik, Moustafa Nawar, Mohamed Sobhy, Seif Kamal Abou Seif, Tarek Khairy, Ahmed Abd El-Aziz, Nasser Taha, Ashraf Reda, Atef Elbahry, Mohamed Setiha, Mohamed Gamal El Din, Magdi Elkhadem, Adel El-Etreby.

South Africa

David Kettles, Junaid Bayat, Heidi Siebert, Adrian Horak, Ynez Kelfkens, Riaz Garda, Barry Jacobson, Thayabran Pillay, Michele Guerra, Louis van Zyl, Hendrik Theron, Andrew Murray, Rikus Louw, Deon Greyling, Pindile Mtla, Siddique Ismail, Fayzal Ahmed, Johannes Engelbrecht, Shambu Maharajh, Wessel Oosthuysen, Rehana Loghdey, Veronica Ueckermann.

United Arab Emirates

Wael Al Mahmeed, Abdullah Al Naemi, Ghazi Yousef, Nooshin Bazargani, Munther AlOmairi, Rajan Maruthanayagam, Rupesh Singh, Ahmed Naguib, Mohamed Ibrahim, Amrish Agrawal, Mukesh Nathani, Ehab M. Esheiba, Adel Wassef, Rajeev Gupta.

United States

Michael Cox, Scott Beach, Peter Duffy, Stephen Falkowski, Kevin Ferrick, Miguel Franco, W. Michael Kutayli, Annette Quick, Niraj Sharma, Vance Wilson, Stephen Miller, Mark Alberts, Edwin Blumberg, Roddy Canosa, Ted Gutowski, Rodney Ison, Jorge Garcia, Paul Mullen, Howard Noveck, Pamela Rama, Rajneesh Reddy, Marcus Williams, Daniel Nishijima, Keith Ferdinand, Ihsan Haque, Robert Mendelson, Sridevi Pitta, Daniel Theodoro, Charles Treasure, Moustafa Moustafa, Cas Cader, Walter Pharr, Alisha Oropallo, George Platt, Jaspal Gujral, James Welker, Firas Koura.