

| Author, year | Type of article: primary study/post hoc or pooled analysis | Aim or objective | Comparison(s) | Outcomes reported | Reason for non-inclusion of data |
|--------------|--|------------------|---------------|-------------------|----------------------------------|
|--------------|--|------------------|---------------|-------------------|----------------------------------|

Randomised comparisons and supporting analyses

| | | | | | |
|--|--------------------------------------|---|---|---|--|
| Pérez-Gómez et al., 2006 ⁴⁵ | Subanalysis of NASPEAF ³⁹ | Subanalysis of high-risk group only according to presence or absence of mitral stenosis | Adjusted-dose acenocoumarol (INR 1.4–2.4) + triflusal (600 mg) vs adjusted-dose acenocoumarol (INR 2.0–3.0) | Same as NASPEAF study ³⁹ | Data reported in the NASPEAF paper ³⁹ includes this subpopulation |
| Pérez-Gómez et al., 2007 ⁴⁴ | Subanalysis of NASPEAF ³⁹ | Subanalysis of according to presence or absence of previous embolism in younger and older population (<75 years vs >75 years) | Acenocoumarol (any INR) + triflusal (600 mg) vs adjusted-dose acenocoumarol (INR 2.0–3.0) | Same as NASPEAF study ³⁹ | Data reported in the NASPEAF paper ³⁹ includes this subpopulation |
| Pérez-Gómez et al., 2007 ⁴⁶ | Review of NASPEAF ³⁹ | Difference in event rates for patients with valvular and non-valvular disease | Acenocoumarol (any INR) + triflusal (600 mg) vs adjusted-dose acenocoumarol (INR 2.0–3.0) | Composite of stroke + TE Bleeding (fatal ICH, GI) | Data reported in the NASPEAF paper ³⁹ includes this subpopulation |
| Gullov et al., 1999 ⁴⁷ | Primary | Analysis of AFASAK II ⁴² | Fixed-dose warfarin (1.25 mg) + aspirin (300 mg) vs fixed-dose warfarin (1.25 mg) or adjusted-dose warfarin (INR 2.0–3.0) | Same as AFASAK II study ⁴² | Duplicate data as the original AFASAK II ⁴² study |
| Blackshear et al., 1999 ⁴⁹ | Subanalysis SPAF III ⁴³ | Incidence of TEE and stroke rates according to plaque presence | Adjusted-dose warfarin (INR 1.2–1.5) + aspirin (325 mg) vs adjusted dose warfarin (INR 2.0–3.0) | Death, TE, bleeding (major) | No new data reported |

Non-randomised comparisons and supporting analyses

| | | | | | |
|--|---------|--|--|--|---|
| Lopes et al., 2009 ⁵⁰ | Primary | Difference in 90-day mortality rates between AF (baseline, new onset and discharge) | Warfarin + aspirin + clopidogrel vs warfarin | Stroke: 90-day rate | Follow-up 90 days Dose of warfarin or APT not specified No. of events not reported for either therapy group (outcomes reported as rate % per patient-year, but no information on patient-year data); no. of participants per therapy group (denominator) not clear |
| Abdelhafiz and Wheelodon, 2008 ⁵¹ | Primary | Assess risk factors for bleeding during long-term anticoagulation of AF in older people (>75 years) in comparison to young people in clinical practice | Adjusted-dose warfarin (INR 2.0–3.0) + aspirin vs adjusted-dose warfarin (INR 2.0–3.0) | Bleeding (major, minor, major + minor) | Only 8 out of 504 patients on combined therapy Follow-up 19 months Dose of aspirin not specified |

| Type of article: primary study/ post hoc or pooled analysis | | Reason for non-inclusion of data | |
|--|---|---|--|
| Author, year | Aim or objective | Comparison(s) | Outcomes reported |
| Amadeus Investigators, 2008 ⁷² | Idraparinux was non-inferior to VKA for primary outcomes | Idraparinux or VKA + aspirin or ticlopidine/clopidogrel vs idraparinux/VKA | Bleeding (any) No. of events not reported for combined therapy group Dose of APT not specified; events not reported separately for idraparinux and VKA in combined therapy arms |
| Suzuki <i>et al.</i> , 2007 ⁵⁶ | Determine incidence and risk factors of major bleeding related to warfarin therapy in Japanese patients | Adjusted-dose warfarin (INR 1.6–2.6) + aspirin vs adjusted-dose warfarin (INR 1.6–2.6) | Bleeding (ICH, major) Dose of aspirin not specified; no. of events in either therapy group not reported (outcomes reported as rate % per-patient-year) |
| Burton <i>et al.</i> , 2006 ⁵⁷ | Compare events in warfarin-treated patients with AF in primary care, with RCT data | Adjusted-dose warfarin (INR 2.0–3.0) + aspirin vs adjusted-dose warfarin (INR 2.0–3.0) | Bleeding (any) Dose of aspirin not specified; very small number of participants on combined therapy ($n = 18$ approx.), no. of patients in either therapy group not clear |
| Stenstrand <i>et al.</i> , 2005 ⁵⁸ | Probability of receiving an OAC at discharge according to background characteristics and other treatments | OAC + aspirin vs OAC | Death (1-year mortality) Name of OAC not reported Dose of aspirin not specified Some patients received combined OAC plus aspirin with or without thienopyridine, but numbers (participants) not clear |
| SPORTIF V investigators, 2005 ⁶⁵ | Whether or not ximelagatran was non-inferior to warfarin | Adjusted-dose warfarin (INR 2.0–3.0) + aspirin (100 mg) vs adjusted-dose warfarin (INR 2.0–3.0) ximelagatran 36 mg (b.i.d.) + aspirin (100 mg) vs ximelagatran 36 mg (b.i.d.) | Bleeding: major + minor No. of patients on individual therapy (denominator) – unclear Only bleeding outcome reported duplicate in another included study ⁶⁹ |
| SPORTIF III Investigators, 2003 ⁶⁴ | Whether or not ximelagatran was non-inferior to warfarin | Adjusted-dose warfarin (INR 2.0–3.0) + aspirin (100 mg) vs adjusted-dose warfarin (INR 2.0–3.0) ximelagatran 36 mg (b.i.d.) + aspirin (100 mg) vs ximelagatran 36 mg (b.i.d.) | Bleeding: major + minor No. of patients on individual therapy (denominator) – unclear Only bleeding outcome reported duplicate in another included study ⁶⁹ |

| Author, year | Type of article: primary study/post hoc or pooled analysis | Aim or objective | Comparison(s) | Outcomes reported | Reason for non-inclusion of data |
|---|--|---|---|--|---|
| White <i>et al.</i> , 2007 ⁶⁸ | Pooled analysis SPORTIF III ⁶⁴ and V ⁶⁵ | Pooled analysis by anticoagulation (INR) control – only patients on warfarin reported | Adjusted-dose warfarin (INR 2.0–3.0) + aspirin (100 mg) vs adjusted-dose warfarin (INR 2.0–3.0) | Bleeding: major Death: all cause Stroke/SE: combined | No. of events not reported for any outcome; event rate % per patient-year reported with no information on either patient-year data or no. of patients (denominator); information on these outcomes also reported in other publication of same studies ⁶⁹ |
| Halperin, 2005 ⁷¹ | Review of SPORTIF III ⁶⁴ and SPORTIF V ⁶⁵ | Thromboembolic risk for patients receiving concomitant aspirin therapy in SPORTIF III ⁶⁴ and V ⁶⁵ with data on SPORTIF III ⁶⁴ only | Adjusted-dose warfarin (INR 2.0–3.0) + aspirin (100 mg) vs adjusted-dose warfarin (INR 2.0–3.0) ximelagatran 36 mg (b.i.d.) + aspirin (100 mg) vs ximelagatran 36 mg (b.i.d.) | Stroke + SE | Data on patients enrolled in SPORTIF III trial ⁶⁴ alone, also reported in another included publication ⁶⁹ ; reporting pooled data for SPORTIF III and V ^{64,65} |
| Douketis <i>et al.</i> , 2006 ⁷⁰ | Pooled analysis of SPORTIF III ⁶⁴ and V ⁶⁵ | Annual incidence of any (major or minor), major, and intracerebral bleeding with ximelagatran and warfarin therapy during the study period, based on the time to first bleeding episode while patients were treated | Adjusted-dose warfarin (INR 2.0–3.0) + aspirin (100 mg) vs adjusted-dose warfarin (INR 2.0–3.0) ximelagatran 36 mg (b.i.d.) + aspirin (100 mg) vs ximelagatran 36 mg (b.i.d.) | Bleeding (major) | No. of events not reported for either therapy group; denominator not reported for combined therapy, outcomes reported as hazard ratios associated with aspirin use |
| Akins <i>et al.</i> , 2007 ⁶⁷ | Pooled analysis of SPORTIF III ⁶⁴ and SPORTIF V ⁶⁵ | Comparison of warfarin and ximelagatran for the secondary prevention of stroke | Adjusted-dose warfarin (INR 2.0–3.0) + aspirin (100 mg) vs adjusted-dose warfarin (INR 2.0–3.0) ximelagatran 36 mg (b.i.d.) + aspirin (100 mg) vs ximelagatran 36 mg (b.i.d.) | Bleeding, stroke- ischaemic/ haemorrhagic and SE | No. of bleeds reported only for patients with previous embolism Data in another included study ⁶⁹ envelopes this patient group |
| Teitelbaum <i>et al.</i> , 2008 ⁶⁶ | Pooled analysis of SPORTIF III ⁶⁴ and SPORTIF V ⁶⁵ | On-treatment analysis of SPORTIF studies to evaluate if treatment with warfarin vs ximelagatran was had a differential effect on cardioembolic vs non-cardioembolic stroke | Adjusted-dose warfarin (INR 2.0–3.0) + aspirin (100 mg) vs adjusted-dose warfarin (INR 2.0–3.0) ximelagatran 36 mg (b.i.d.) + aspirin (100 mg) vs ximelagatran 36 mg (b.i.d.) | Bleeding (primary brain haemorrhage) Stroke (all – clinical types: cardioembolic, non- cardioembolic, uncertain) | No. of patients on individual therapy (denominator) – unclear; stroke outcomes reported in another included study ⁶⁹ |

| Author, year | Type of article: primary study/post hoc or pooled analysis | Aim or objective | Comparison(s) | Outcomes reported | Reason for non-inclusion of data |
|---|--|--|---|---------------------------|--|
| Johnson <i>et al.</i> , 2005 ⁵⁹ | Primary | Annual rate of major haemorrhage in previously hospitalised patients on warfarin | Adjusted-dose warfarin (INR 2.0–3.0) + APT vs adjusted-dose warfarin (INR 2.0–3.0) | Bleeding: major | Name of APT not specified; no. of participants not reported for combined therapy group; <i>n</i> = 228 |
| Blich and Gross, 2004 ⁶¹ | Primary | Incidence of thromboembolic and bleeding events in patients with AF | Adjusted-dose warfarin (INR 2.0–3.0) + aspirin (100 mg) vs adjusted-dose warfarin (INR 2.0–3.0) | Bleeding: TE | No. of participants not reported for individual therapy arms, data reported as event rate % per patient-year |
| Shireman <i>et al.</i> , 2004 ⁶⁰ | Primary | Influence of patient-specific factors on concomitant warfarin–antiplatelet therapy and potential impact of combined therapy on bleeding risk | Warfarin + aspirin/clopidogrel/ticlopidine/dual APT vs warfarin | Bleeding (ICH, major, GI) | Dose of warfarin or APT not specified, outcomes not reported for combination of warfarin with individual APT separately |
| Klein <i>et al.</i> , 2003 ⁶² | Primary | To calculate cumulative major, minor and composite bleeding rates for the 56-day study period | Adjusted-dose warfarin (INR 2.0–3.0)/heparin + aspirin vs adjusted-dose warfarin (INR 2.0–3.0) | Bleeding (major) | Follow-up 56 days; dose of aspirin not specified; no. of events in combined therapy group not clear; outcomes not reported separately for warfarin + aspirin and heparin + aspirin |
| Toda <i>et al.</i> , 1998 ⁵² | Primary | Relationship between incidence of TE in patients with AF, and (1) underlying disease; (2) type of AF; and (3) antithrombotic therapy | Warfarin + APT vs warfarin | TE | <i>n</i> = 257; dose of warfarin or APT not specified; name of APT in combined therapy arm not reported; no. of participants in individual therapy groups not clear |
| Albers <i>et al.</i> , 1996 ⁵³ | Primary | Assess current status of antithrombotic therapy for patients with AF | Adjusted-dose warfarin (INR 2.0–3.0) + aspirin vs adjusted-dose warfarin (INR 2.0–3.0) | Bleeding (per rectum) | <i>n</i> = 309, follow-up period not reported; dose of aspirin in combined therapy group not reported; definition of bleeding possibly different in either therapy group |

b.i.d., dose administered twice daily; GI, gastrointestinal; OT, on treatment; TEE, transoesophageal echocardiography.