

### Supplementary appendix 3. Characteristics of the included studies and treatment arms.

#### Characteristics of the included studies.

| Study                      | Sample size | Geographic region | Qualifying event  | Dose(mg)                          | Age(mean, range/SD) | Male (%) | Hypertension (%) | Diabetes (%) | Smoking(%) | Event to enrollment | Average follow-up period(y) |
|----------------------------|-------------|-------------------|-------------------|-----------------------------------|---------------------|----------|------------------|--------------|------------|---------------------|-----------------------------|
| 1977 AITIA (27)            | 319         | USA               | TIA               | A1300 vs. P                       | 45-74(85%)*         | 62       | 44               | 12           | 52         | <3m                 | 1.42                        |
| 1978 Canadian Coop (28)    | 283         | Canada            | TIA/IS            | A1300 vs. P                       | —                   | 68       | —                | —            | —          | <3 m                | 2.17                        |
| 1982 Guiraud-Chaumeil (29) | 440         | —                 | IS/TIA            | A990 vs. A990 + D150 vs. P        | 62                  | 85       | —                | —            | —          | —                   | 2.83                        |
| 1983 AICLA (30)            | 604         | France            | IS/TIA            | A990 vs. A990 + D225 vs. P        | 63±10               | 70       | 63               | 22           | 64         | <12 m               | 3.00                        |
| 1983 Danish coop (31)      | 203         | Denmark           | TIA/RIND          | A1000 vs. P                       | 59(34-75)           | 73       | 27               | NA           | 73         | <1 m                | 2.08                        |
| 1984 Tohgi (32)            | 340         | Japan             | IS/TIA            | A500 vs. TC                       | —                   | —        | —                | —            | —          | —                   | 1.00                        |
| 1985 ACCSG (33)            | 890         | USA/Canada        | IS/TIA            | A1300 vs. A1300 + D300            | 63(41-80)†          | 67       | 43               | 15           | —          | <3 m(94%)¶          | 2.50                        |
| 1987 Swedish Coop (34)     | 505         | Sweden            | IS                | A1500 vs. P                       | 68(27-93)           | 62       | 46               | 17           | 52         | <3w                 | 2.00                        |
| 1989 CATS (35)             | 1072        | Canada            | IS                | TC500 vs. P                       | 65                  | 62       | 68               | 32           | 37§        | <4 m                | 2.33                        |
| 1989 TASS (36)             | 3069        | North America     | TIA/RIND/minor IS | A1300 vs. TC500                   | 63±9 (39-94)        | 65       | 39               | 20           | 42§        | <3 m                | 3.50                        |
| 1990 ESPS (37)             | 2500        | Europe            | TIA/RIND/IS       | A990 + D225 vs. P                 | 64                  | 58       | 37               | —            | 43         | <3 m                | 1.92                        |
| 1991 Dutch TIA (38)        | 3131        | Europe            | TIA/ minor IS     | A30 vs. A283                      | >65(54%)‡           | 65       | 42               | 8            | 45§        | ≤3 m                | 2.58                        |
| 1991 SALT (39)             | 1360        | Sweden            | TIA/minor IS/RAO  | A75 vs. P                         | 67(50-79)           | 66       | 48               | 13           | 50         | <4 m                | 2.67                        |
| 1991 UK-TIA (40)           | 2435        | UK                | TIA/small IS      | A300 vs. A1200 vs. P              | 60(≥40)             | 63       | 27               | 4            | 53         | <4 m                | 4.17                        |
| 1996 CAPRIE stroke (41)    | 6428        | —                 | IS                | A325 vs. C75                      | 65±11               | 64       | 65               | 26           | 65         | 1w-6m               | 1.19                        |
| 1996 ESPS2 (42)            | 6602        | Europe            | IS TIA            | A50 vs. A50 + D400 vs. D400 vs. P | 67(>18)             | 58       | 61               | 15           | 24§        | <3 m                | 2.00                        |
| 1998 Alvarez Sabín (43)    | 217         | Spain             | IS                | A330 vs. TF900                    | 43                  | 81       | 31               | —            | —          | —                   | 3.92                        |
| 2000 CSPS (44)             | 1067        | Japan             | IS                | CL200 vs. P                       | 65(36-80)           | 66       | 61               | 25           | —          | 1-6 m               | 1-5                         |

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|---|-------|-----------------------------------|--------------|-------------------------------------|------------|----|----|----|-----|--------|------|
| 2003 AAASPS (45)                        | 1809  | USA                               | IS           | A650 vs. TC500                      | 61(29-85)  | 46 | 85 | 41 | 63  | 1w-3m  | 1.54 |
| 2003 TOPALS (46)                        | 270   | Japan                             | IS/TIA       | A81 + TC100 vs. TC200               | 67(>40)    | 65 | 47 | 23 | 33  | <6 m   | 1.59 |
| 2003 TACIP (47)                         | 2107  | Portugal/Spain                    | IS/TIA       | A325 vs. TF600                      | 65(≥40)    | 66 | 61 | 24 | 31  | <6 m   | 2.51 |
| 2004 TAPIRSS (48)                       | 429   | Argentina                         | IS/TIA       | A325 vs. TF600                      | 65(>40)    | 68 | 71 | 18 | 53  | <6 m   | 1.63 |
| 2004 MATCH (49)                         | 7599  | Worldwide                         | IS/TIA       | A75 + C75 vs. C75                   | 66±10(≥40) | 63 | 78 | 68 | 47  | ≤3 m   | 1.50 |
| 2006 ESPRIT (50)                        | 2739  | Worldwide                         | TIA/minor IS | A75(median) vs. A75(media n) + D400 | 63±11      | 66 | 60 | 19 | 37§ | ≤6 m   | 3.50 |
| 2007 FASTER (51)                        | 392   | Canada                            | minor IS     | A81 vs. A81 + C75                   | 68(≥40)    | 53 | 51 | 11 | 26§ | ≤24h   | 0.25 |
| 2008 Fukuuchi (52)                      | 1151  | Japan                             | IS           | C75 vs. TC200                       | 65(20-80)  | 73 | 68 | 19 | 63  | ≥8d    | 1.00 |
| 2008 CASISP (53)                        | 719   | China                             | IS           | A100 vs. CL200                      | 60         | 69 | 79 | 18 | —   | <6 m   | 1.00 |
| 2008 PRoFESS (54)                       | 20332 | Worldwide                         | IS           | A50 + D400 vs. C75                  | 66(≥55)    | 64 | 74 | 28 | 57  | <3 m   | 2.50 |
| 2009 Uchiyama Phase IIIa (55)           | 711   | Japan                             | IS           | C75 vs. TC200                       | 65(20-80)  | 69 | 70 | 25 | 37  | ≥8d    | 0.50 |
| 2010 CSPS2 (56)                         | 2672  | Japan                             | IS           | A81 vs. CL200                       | 64(20-79)  | 72 | 74 | 29 | 29§ | <6.5 m | 2.42 |
| 2011 CHARISMA stroke and TIA group (57) | 4320  | Worldwide                         | IS/TIA       | A75-162 vs. A75-162 + C75           | 65(≥45)    | 63 | 76 | 29 | 19§ | <60 m  | 2.08 |
| 2011 TOSS2 (58)                         | 457   | East Asia                         | IS           | A70-150 + C75 vs. A70-150 + CL200   | 65(≥35)    | 51 | 72 | 43 | 42  | ≤2w    | 0.58 |
| 2011 CAIST (59)                         | 458   | Japan                             | IS           | A300 vs. CL200                      | 63(31-85)  | 61 | 65 | 35 | 41  | ≤48h   | 0.25 |
| 2011 JASAP (60)                         | 1291  | Japan                             | IS           | A81 vs. A50 + D400                  | 66(≥50)    | 72 | 88 | 40 | 68  | 1w-6m  | 1.25 |
| 2012 SPS3 (61)                          | 3020  | North America/Latin America/Spain | lacunar IS   | A325 vs. A325 + C75                 | 63(≥30)    | 63 | 75 | 37 | 20§ | <6 m   | 3.40 |
| 2013 ECLIPse (62)                       | 203   | Japan                             | lacunar IS   | A100 vs. A100 + CL200               | 65(≥45)    | 75 | 57 | 29 | 32§ | ≤7d    | 0.25 |

TIA, transient ischemic attack; IS, ischemic stroke; RIND, reversible ischemic neurologic deficit; RAO, Retinal artery occlusion; A, aspirin; D, dipyridamole; P, placebo; TF, triflusal; TC, ticlopidine; CL, cilostazol; C, clopidogrel; SD, standard deviation; y, years; m, months; d, days; h, hours; doses in mg/day are shown; — indicates that data is not available; \* 45-74 years old for 85% included patients; † 41-80 years old for 95% included patients; ‡ > 65 years old for 53% included patients; §current smoking ; ¶ within three months for 94% included patients.

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#### Number of trials, patients and events by intervention.

| Regimens | Serious vascular events |                 |                              |        | Recurrent stroke |                 |                              |        | Any bleeding  |                 |                              |        | Discontinuation due to adverse events |                 |                              |        |
|----------|-------------------------|-----------------|------------------------------|--------|------------------|-----------------|------------------------------|--------|---------------|-----------------|------------------------------|--------|---------------------------------------|-----------------|------------------------------|--------|
|          | No. of trials           | No. of patients | of Follow-up (patient years) | Events | No. of trials    | No. of patients | of Follow-up (patient years) | Events | No. of trials | No. of patients | of Follow-up (patient years) | Events | No. of trials                         | No. of patients | of Follow-up (patient years) | Events |
| P        | 12                      | 6482            | 16075                        | 1407   | 12               | 6482            | 16075                        | 954    | 9             | 4974            | 13022                        | 168    | 10                                    | 6187            | 15332                        | 409    |
| D        | 1                       | 1654            | 3308                         | 297    | 1                | 1654            | 3308                         | 211    | 1             | 1654            | 3308                         | 77     | 1                                     | 1654            | 3308                         | 249    |
| A1       | 2                       | 3204            | 7341                         | 521    | 1                | 1649            | 3298                         | 206    | 2             | 3204            | 7341                         | 224    | 2                                     | 3204            | 7310                         | 216    |
| A2       | 8                       | 6845            | 15583                        | 800    | 8                | 6845            | 15583                        | 561    | 8             | 6845            | 15583                        | 849    | 6                                     | 4579            | 11058                        | 395    |
| A3       | 8                       | 8686            | 19855                        | 1284   | 6                | 3915            | 11956                        | 402    | 7             | 5491            | 16053                        | 538    | 4                                     | 2825            | 7836                         | 220    |
| A4       | 11                      | 4879            | 13729                        | 966    | 10               | 4709            | 13559                        | 564    | 8             | 4461            | 12933                        | 311    | 8                                     | 4418            | 12830                        | 594    |
| AD1      | 4                       | 13846           | 34338                        | 1783   | 4                | 13846           | 34338                        | 1238   | 4             | 13846           | 34338                        | 906    | 4                                     | 13846           | 34338                        | 2339   |
| AD2      | 4                       | 2037            | 4514                         | 304    | 3                | 1900            | 4126                         | 178    | 2             | 650             | 1726                         | 38     | 3                                     | 1900            | 4126                         | 269    |
| TC       | 7                       | 4193            | 9118                         | 659    | 6                | 4023            | 8948                         | 394    | 5             | 3678            | 8775                         | 204    | 5                                     | 3885            | 8728                         | 645    |
| A+TC     | 1                       | 132             | 210                          | 10     | 1                | 132             | 210                          | 7      | 1             | 132             | 210                          | 6      | —                                     | —               | —                            | —      |
| C        | 5                       | 18125           | 35684                        | 2288   | 4                | 14892           | 31837                        | 1273   | 3             | 14526           | 31654                        | 563    | 3                                     | 11090           | 26134                        | 1203   |
| A+C      | 5                       | 7894            | 15520                        | 799    | 5                | 7894            | 15520                        | 590    | 5             | 7894            | 15520                        | 1178   | 1                                     | 198             | 50                           | 17     |
| TF       | 3                       | 1374            | 3411                         | 189    | 3                | 1374            | 3411                         | 142    | 3             | 1374            | 3411                         | 154    | 1                                     | 213             | 347.19                       | 5      |
| CL       | 4                       | 2461            | 5252                         | 158    | 4                | 2461            | 5252                         | 133    | 4             | 2461            | 5252                         | 83     | 4                                     | 2461            | 5252                         | 380    |
| A+CL     | 2                       | 322             | 160                          | 16     | 2                | 332             | 160                          | 12     | 2             | 332             | 160                          | 3      | —                                     | —               | —                            | —      |

A, aspirin; D, dipyridamole; P, placebo; TF, triflusal; TC, ticlopidine; CL, cilostazol; C, clopidogrel; A1, aspirin 30-50 mg daily; A2, aspirin 75-162 mg daily; A3, aspirin 283-330 mg daily; A4, aspirin 500-1500 mg daily; AD1, aspirin 50 mg plus dipyridamole 400 mg daily; AD2, aspirin 990-1300 mg plus dipyridamole 150-300 mg daily; — indicates that data is not available.