Appendix Table C8. Study withdrawals and adverse events (outcomes Part D), ACEI monotherapy versus control treatment trials

| **Study** | **Any Study Withdrawals** | | **Any or Serious Adverse Events Leading to Study Withdrawal** | | **Adverse Event:**  **Cough** | | | **Adverse Event:**  **Hyperkalemia** | | | **Renal Adverse Events**  **Leading to Withdrawal\*** | | **Renal Adverse Events** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ACEI** | **Control** | **ACEI** | **Control** | **ACEI** | **Control** | | **ACEI** | **Control** | | **ACEI** | **Control** | **ACEI** | **Control** |
| ***ACEI versus placebo/no treatment trials (n=17)*** | | | | | | | | | | | | | | |
| Perkovic, 20071  (PRGRESS) |  |  |  |  |  |  | |  |  | |  |  |  |  |
| Asselbergs, 20042  (PREVD) | 103/431 (24) | 110/433 (25.4) |  |  |  |  | |  |  | |  |  |  |  |
| Marre, 20043  (DIAB) | 334/2443  (13.7)\*\* | 324/2469  (13.1)\*\* | 609/2443  (24.9) | 554/2469  (22.4) | 80/2443  (3.3) | 21/2469  (0.9) | |  |  | |  |  |  |  |
| Katayama, 20024 | 12/52  (23.1) | 10/27  (37) | 2/52  (3.8) | 1/27  (3.7) |  |  | |  |  | |  |  |  |  |
| Bojestig, 20015 | 4/37  (10.8) | 0/18 | 3/37  (8.1) | 0/18 | 1/37  (2.7) | 0/18 | |  |  | |  |  |  |  |
| Gerstein, 20016  (MICROHOPE) |  |  |  |  |  |  | |  |  | |  |  |  |  |
| O’Hare, 20007  (ATLANTIS) | 31/92  (33.7) | 11/48  (22.9) | 15/92  (16.3) | 5/48  (10.4) |  |  | |  |  | |  |  |  |  |
| Muirhead, 19998 | 4/29  (13.8) | 7/31  (22.6) | 2/29  (6.9) | 0/31 | 6/29  (20.7) | 1/31  (3.2) | |  |  | |  |  |  |  |
| REIN, 19999 11  Stratum 1 | 20/99  (20.2)† | 20/87  (23)† | 11/99  (11.1) | 6/87  (6.9) | 1/99  (1.0) | 0/87 | | 0/99 | 1/87  (1.1) | | 1/99  (1.0) | 0/87 | Worsening renal insufficiency |  |
| Crepaldi, 199810 | 2/32  (6.3) | 6/34  (17.6) | 1/32  (3.1) | 6/34  (17.6) |  |  | |  |  | | 0/32 | 1/34  (2.9) | Diabetic nephropathy |  |
| REIN, 199711  Stratum 2 | 14/78  (17.9) † | 21/88  (23.9) † | 9/78  (11.5) | 11/88  (12.5) |  |  | | 1/78  (1.3) | 1/88  (1.1) | | 0/78 | 2/88  (2.3) | Worsening renal insufficiency |  |
| Maschio, 199612 | 68/300  (22.7) | 61/283  (21.6) | 52/300  (17.3) | 41/283  (14.5) | 25/300  (8.3) | 10/283  (3.5) | | 5/300  (1.7) | 3/283  (1.1) | | 3/300  (1.0) | 6/283  (2.1) | Worsening renal insufficiency |  |
| Trevisan, 199513 | 6/60  (10) | 8/62  (12.9) | 4/60  (6.7) | 7/62  (11.3) | 1/60  (1.7) | 1/62  (1.6) | |  |  | |  |  |  |  |
| Laffel, 199514 | 22/70  (31.4) | 21/73  (28.8) | 4/70  (5.7) | 5/73  (6.8) | 15/70  (21.4) | 16/73  (21.9) | | 0/70 | 0/73 | |  |  |  |  |
| Sano, 199415 |  |  | 0/26 | 0/26 | 0/26 | 0/26 | | 0/26 | 0/26 | |  |  |  |  |
| Lewis, 199316 |  |  | 46/207  (22.2) | 58/202  (28.7) |  |  | | 3/207  (1.4) | 0/202 | |  |  |  |  |
| Appendix Table C8. Study withdrawals and adverse events (outcomes Part D), ACEI monotherapy versus control treatment trials (continued) | | | | | | | | | | | | | | |
| **Study** | **Any Study Withdrawals** | | **Any or Serious Adverse Events Leading to Study Withdrawal** | | **Adverse Event:**  **Cough** | | | **Adverse Event:**  **Hyperkalemia** | | | **Renal Adverse Events**  **Leading to Withdrawal\*** | | **Renal Adverse Events** | |
| **ACEI** | **Control** | **ACEI** | **Control** | **ACEI** | **Control** | | **ACEI** | **Control** | | **ACEI** | **Control** | **ACEI** | **Control** |
| Ravid, 199317 | 3/56  (5.3) | 3/52  (5.8) | 4/56  (7.1) | 3/52  (5.8) | 4/56  (7.1) | 2/52  (3.8) | |  |  | |  |  |  |  |
| ***ACEI versus ARB trials (n=6)*** | | | | | | | | | | | | | | |
| Mann, 200818  ONTARGET |  |  |  |  |  |  | |  |  | |  |  |  |  |
| Menne, 200819  VALERIA | 6/47  (12.8) | 6/43  (14.0) | 4/47  (8.5) | 3/43  (7) | 2/47  (4.3) | 0/43 | | 1/47  (2.1) | 1/43  (2.3) | |  |  |  |  |
| Sengul, 200620 | 15/109  (13.8) | 12/110  (10.9) |  |  |  |  | |  |  | |  |  |  |  |
| Barnett, 200421  DETAIL | 44/130  (33.8) | 38/120  (31.7) | 30/130  (23.1) | 20/120  (16.7) |  |  | |  |  | | 2/130  (1.5) | 2/120  (1.7) | Elevated serum creatinine | |
| Lacourcière, 200022 | 5/51  (9.8) | 6/52  (11.5) | 1/51  (2) | 2/52  (3.8) | 7/51  (13.7) | 0/52 | |  |  | |  |  |  |  |
| Muirhead, 19998 | 4/29  (13.8) | 8/62  (12.9) | 2/29  (6.9) | 2/62  (3.2) | 6/29  (20.7) | 4/62  (6.5) | |  |  | | 0/29  0 | 1/62  (1.6) | Decreased GFR and creatinine clearance | |
| ***ACEI versus CCB trials (n=5)*** | | | | | | | | | | | | | | |
| Rahman, 200634  ALLHAT |  |  |  |  |  |  | |  |  | |  |  |  |  |
| Fogari, 200224 | 26/102  (25.5) | 27/103  (26.2) | 3/102  (2.9) | 4/103  (3.9) | 2/102  (2.0) | 0/103 | |  |  | | 2/102  (2.0) | 2/103  (1.9) | Worsening kidney function | |
| Wright, 200226  (AASK) | 0/436 | 0/217 | 0/436 | 0/217 | 54.9\* | 46.3\* | | 3/436  (0.7) | 0/217 | |  |  |  |  |
| Wright, 200226  (AASK) | Other adverse events that were significantly different between groups (p<0.5): angioedema ACE 6.4\* vs. 2.3\* for CCB; Syncope ACE 6.7\* vs. 2.3\* for CCB; Edema ACE 46\* vs. 59.8\* for CCB | | | | | | | | | | | | | |
| Marin, 200128  ESPIRAL | 45/129  (34.9) | 38/112  (33.9) | 15/129  (11.6) | 12/112  (10.7) | 3/129  (2.63) | 0/112 | |  |  | | 4/129  (3.1) | 1/112  (0.9) | Impaired kidney function | |
| Crepaldi, 199810 | 17/47  (36.2) | 17/41  (41.2) | 1/32  (3.1) | 0/26 |  |  | |  |  | | 0/32 | 0/26 |  |  |
| Zucchelli, 199529 | 15/60  (25) | 16/61  (26) | 5/60  (8.3) | 7/61  (11.5) | 2/60  (3.3) | 0/61 | |  |  | |  |  |  |  |
| ***ACEI versus BB trials (n=3)*** | | | | | | | | | | | | | | |
| Wright, 200226 (AASK) | 0/436 | 0/441 | 0/436 | 0/441 | 54.9\* | 41.5\* | | 3/436  (0.7) | 1/441  (0.2) | |  |  |  |  |
| van Essen, 199731 | 9/52  (17.3) | 5/51  (9.8) | 9/52  (17.3) | 5/51  (9.8) |  |  | | 1/52  (1.9) | 0/51 | |  |  |  |  |
| Hannedouche, 199432 | 11/52  (21.2) | 12/48  (25.0) | 3/52  (5.8) | 3/48  (6.3) |  |  | | 2/52  (3.8) | 0/48 | |  |  |  |  |
| ***ACEI versus diuretics (n=2)*** | | | | | | | | | | | | | | |
| Rahman, 200634  ALLHAT |  |  |  |  |  | |  |  | |  |  |  |  |  |
| Marre, 200433  NESTOR | 30/286  (10.5) | 35/284  (12.3) | 15/286  (5.2) | 14/284  (4.9) |  | |  |  | |  |  |  |  |  |

\* Results reported as percent of patients experiencing adverse event per patient year of followup (patients were followed up for 3 to 6.4 years)  
ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor II blocker; CCB = calcium channel blocker; BB = beta blocker