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 11Stratum 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, 199711Stratum 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, 200818ONTARGET |  |  |  |  |  |  |  |  |  |  |  |  |
| Menne, 200819VALERIA | 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, 200421DETAIL | 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) |  |  | 0/290 | 1/62(1.6) | Decreased GFR and creatinine clearance |
| ***ACEI versus CCB trials (n=5)*** |
| Rahman, 200634ALLHAT |  |  |  |  |  |  |  |  |  |  |  |  |
| 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, 200128ESPIRAL | 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, 200634ALLHAT |  |  |  |  |  |  |  |  |  |  |  |  |
| Marre, 200433NESTOR | 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