**Supplementary material**

**Table S1-1 Characteristics of included studies**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **PCSK9 inhibitors** | **control** | **Mean age(years)** | |  | **No. of patients** | |  | **Follow**  **up(weeks)** |
| **PCSK9 inhibitors** | **control** | **PCSK9 inhibitors** | **control** |
| **ODYSSEY ALTERNATIVE [S1]** | alirocumab  150mg/2W | ezetimibe | 64.1±9.0 | 62.8±10.1 |  | 126 | 125 |  | 24 |
| **ODYSSEY CHOICE I [S2]** | alirocumab  300mg/4W | placebo | 61.6±10.0 | 61.6±9.7 |  | 312 | 157 |  | 24 |
| **ODYSSEY CHOICE II [S3]** | alirocumab  75mg/2W | placebo | 62.5±9.9 | 63.1±10.7 |  | 116 | 58 |  | 32 |
| **ODYSSEY COMBO I [S4]** | Alirocumab  75mg/2W | placebo | 63.0±9.5 | 63.0±8.8 |  | 209 | 107 |  | 52 |
| **ODYSSEY COMBO II [S5]** | Alirocumab  75mg/2W | ezetimibe | 61.7±9.4 | 61.3±9.2 |  | 479 | 241 |  | 52 |
| **ODYSSEY DM-DYSLIPIDEMIA [S6]** | Alirocumab  75-150mg/2W | Usual care | 62.8±9.3 | 64.1±8.8 |  | 276 | 137 |  | 24 |
| **ODYSSEY DM-INSULIN [S7]** | Alirocumab  150mg/2W | Placebo | 63.9±8.9 | 64.0±9.4 |  | 294 | 147 |  | 24 |
| **ODYSSEY ESCAPE [S8]** | Alirocumab  75-150mg/2W | Placebo | 59.5±9.2 | 57.0±10.5 |  | 41 | 21 |  | 18 |
| **ODYSSEY FH I [S9]** | Alirocumab  75-150mg/2W | Placebo | 52.1±12.9 | 51.7±12.3 |  | 322 | 163 |  | 24 |
| **ODYSSEY FH II [S9]** | Alirocumab  75-150mg/2W | Placebo | 53.2±12.9 | 53.2±12.5 |  | 167 | 82 |  | 24 |
| **ODYSSEY HIGH FH [S10]** | Alirocumab  150mg/2W | Placebo | 49.8±14.2 | 52.1±11.2 |  | 72 | 35 |  | 24 |

**Table S1-2 Characteristics of included studies**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **PCSK9 inhibitors** | **control** | **Mean age(years)** | |  | **No. of patients** | |  | **Follow**  **up(weeks)** |
| **PCSK9 inhibitors** | **control** | **PCSK9 inhibitors** | **control** |
| **ODYSSEY JAPAN [S11]** | alirocumab  75-150mg/2W | placebo | 60.3±9.7 | 61.8±9.0 |  | 144 | 72 |  | 24 |
| **ODYSSEY KT [S12]** | alirocumab  75-150mg/2W | placebo | 61.2±10.4 | 60.1±9.1 |  | 97 | 102 |  | 24 |
| **ODYSSEY LONG TERM [S13]** | alirocumab  150mg/2W | placebo | 60.4±10.4 | 60.6±10.4 |  | 1553 | 788 |  | 78 |
| **ODYSSEY MONO [S14]** | Alirocumab  75mg-150/2W | Ezetimibe  10mg/d | 60.8±4.6 | 59.6±5.3 |  | 52 | 51 |  | 24 |
| **ODYSSEY OPTIONS I [S15]** | Alirocumab  75mg-150mg/2W | Ezetimibe  10mg/d | 62.2±10.0 | 65.7±9.0 |  | 57 | 55 |  | 24 |
| **ODYSSEY OPTIONS II [S16]** | Alirocumab  75mg-150mg/2W | Ezetimibe  10mg/d | 62.2±11.1 | 60.4±10.4 |  | 49 | 48 |  | 24 |
| **ODSSEY OUTCOMES [S17]** | Alirocumab  75mg-150mg/2W | placebo | 58.5±9.3 | 58.6±9.4 |  | 9462 | 9462 |  | 134 |
| **McKenney JM [S18]** | Alirocumab  150mg/2W | placebo | 59.9±11.1 | 53.3±8.5 |  | 31 | 31 |  | 12 |
| **Teramoto T [S19]** | Alirocumab  150mg/2W | placebo | 58.2±8.8 | 58.6±9.2 |  | 25 | 25 |  | 12 |
| **Stein EA [S20]** | Alirocumab  150mg/2W | placebo | 56.3±10.2 | 51.9±9.6 |  | 16 | 15 |  | 12 |
| **Roth EM [S21]** | Alirocumab  NR | placebo | 57.6±9.3 | 55.3±10.3 |  | 30 | 31 |  | 8 |

**Table S1-3 Characteristics of included studies**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **PCSK9 inhibitors** | **control** | **Mean age(years)** | |  | **No. of patients** | |  | **Follow**  **up(weeks)** |
| **PCSK9 inhibitors** | **control** | **PCSK9 inhibitors** | **control** |
| **LAPLACE-TIMI 57 [S22]** | Evolocumab 140mg/2W | placebo | 63.5 | 61.0 |  | 78 | 78 |  | 12 |
| **MENDEL [S23]** | Evolocumab 140mg/2W | placebo | 52.8±11.6 | 52.5±9.8 |  | 45 | 45 |  | 12 |
| **DESCARTES [S24]** | Evolocumab 420mg/4W | placebo | 55.9±10.8 | 56.7±10.1 |  | 599 | 302 |  | 52 |
| **EBBINGHAUS [S25]** | Evolocumab 140mg/2W | placebo | 62.9±8.7 | 62.7±8.7 |  | 983 | 990 |  | 24 |
| **FOURIER [S26]** | Evolocumab  140mg/2W or  420mg/4W | placebo | 62.5±9.1 | 62.5±8.9 |  | 13784 | 13780 |  | 105 |
| **GAUSS [S27]** | Evolocumab  420mg/4W | placebo | 62.0±7.2 | 62.4±6.6 |  | 30 | 32 |  | 12 |
| **GAUSS-2 [S28]** | Evolocumab 140mg/2W | Ezetimibe  10mg/d | 61.0±10.0 | 62.0±10.0 |  | 103 | 51 |  | 12 |
| **GAUSS-3 [S29]** | Evolocumab 420mg/4W | Ezetimibe  10mg/d | 59.0±11.1 | 58.5±9.4 |  | 145 | 73 |  | 24 |
| **GAUSS-4 [S30]** | Evolocumab 140mg/2W or  420mg/4W | Ezetimibe 10mg/d | 65.8±9.8 | 61.8±11.9 |  | 40 | 41 |  | 12 |
| **GLAGOV [31]** | Evolocumab 420mg/4W | placebo | 59.8±9.6 | 59.8±8.8 |  | 484 | 484 |  | 76 |
| **OSLER [32]** | Evolocumab  420mg/4W | placebo | 57.8±11.0 | 58.2±10.9 |  | 2976 | 1489 |  | 48 |

**Table S1-4 Characteristics of included studies**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **PCSK9 inhibitors** | **control** | **Mean age(years)** | |  | **No. of patients** | |  | **Follow**  **up(weeks)** |
| **PCSK9 inhibitors** | **control** | **PCSK9 inhibitors** | **control** |
| **YUKAWA [S33]** | Evolocumab 140mg/2W | placebo | 60.8±9.2 | 60.2±10.1 |  | 52 | 52 |  | 12 |
| **YUKAWA-2 [S34]** | Evolocumab 140mg/2W | placebo | 61.8±11.9 | 60.4±10.4 |  | 51 | 52 |  | 12 |
| **EVOPACS [S35]** | Evolocumab 140mg/2W | placebo | 60.5±12.0 | 61.0±10.7 |  | 155 | 153 |  | 8 |
| **LAPLACE-2 [S36]** | Evolocumab 140mg/2W or  420mg/4W | placebo | 59.6±9.9 | 59.9±10.2 |  | 1117 | 558 |  | 12 |
| **MENDEL-2 [S37]** | Evolocumab 140mg/2W | placebo | 53.0±14 | 54.0±10 |  | 153 | 76 |  | 12 |
| **RUTHERFORD [S38]** | Evolocumab 420mg/4W | placebo | 51.8±13 | 49.3±11.3 |  | 56 | 56 |  | 12 |
| **RUTHERFORD-2 [S39]** | Evolocumab  140mg/2W | placebo | 52.6±12.3 | 51.1±14.2 |  | 110 | 54 |  | 12 |
| **TESLA Part B [S40]** | Evolocumab 420mg/4W | placebo | 30.0±12.0 | 32.0±14.0 |  | 33 | 16 |  | 12 |
| **ANITSCHKOW [S41]** | Evolocumab  420mg/4W | placebo | 60.0±6.8 | 60.7±7.6 |  | 65 | 64 |  | 12 |
| **FLOREY [S42]** | Evolocumab 420mg/2W | placebo | 33.5±11.6 | 33.9±12.7 |  | 23 | 22 |  | 8 |
| **SPIRE [S43]** | Bococizumab  150mg/2W | placebo | 62.9 | 63.0 |  | 13720 | 13718 |  | 40 |

**Table S1-5 Characteristics of included studies**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **PCSK9 inhibitors** | **control** | **Mean age(years)** | |  | **No. of patients** | |  | **Follow**  **up(weeks)** |
| **PCSK9 inhibitors** | **control** | **PCSK9 inhibitors** | **control** |
| **Ridker PM [S44]**  **SPIRE-HR**  **SPIRE-LDL**  **SPIRE-FH**  **SPIRE-LL**  **SPIRE-SI**  **SPIRE-AI** | Bococizumab  150mg/2W  Bococizumab  150mg/2W  Bococizumab  150mg/2W  Bococizumab  150mg/2W  Bococizumab  150mg/2W  Bococizumab  75-150mg/2W | Placebo  Placebo  Placebo  Placebo  Placebo  placebo | 61.1±10.2  61.8±9.3  56.5±10.5  61.5±9.9  64.0±9.2  60.0±10.0 | 61.5±9.7  62.2±9.8  55.7±11.2  61.7±10.0  63.2±8.4  61.0±11.0 |  | 357  1068  185  499  74  200 | 354  1071  185  247  73  99 |  | 58  58  58  58  58  18 |
| **Yokote K [S45]** | Bococizumab 150mg/2W | placebo | 59.6±8.6 | 58.2±11.2 |  | 22 | 26 |  | 16 |

**NR, no reported**

**Table S2 Search terms used for meta-analysis in MEDLINE, Cochrane Library database and Clinicaltrials.gov**

|  |  |
| --- | --- |
| **Concept** | **Search terms** |
| **PCSK9 inhibitors** | **‘evolocumab’ or ‘AMG 145’ or ‘alirocumab’ or ‘SAR236553’ or ‘REGN727’ or ‘bococizumab’ or ‘RN316/PF-04950615’.** |

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