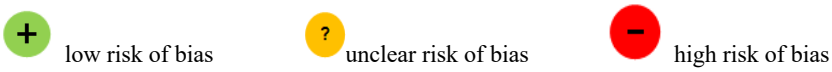
# Supplementary data

**Supplementary Table 1 – Risk of bias in included trials**

| | Random sequence generation | Allocation concealment | Blinding of participants/ personnel | Blinding of outcome assessor | Incomplete outcome data | Selective Reporting |
|---|---|---|---|---|---|---|
| Ballantyne et al. 2018 (CLEAR Tranquility) | + | + | + | + | + | + |
| Ballantyne et al. 2019 | ? | + | + | + | + | + |
| Goldberg et al. 2019 (CLEAR Wisdom) | + | + | + | + | + | + |
| Gutierrez et al. 2014 | ? | ? | + | ? | + | + |
| Laufs et al. 2019 (CLEAR Serenity) | ? | + | + | + | + | + |
| Ray et al. 2019 (CLEAR Harmony) | + | + | + | + | + | + |



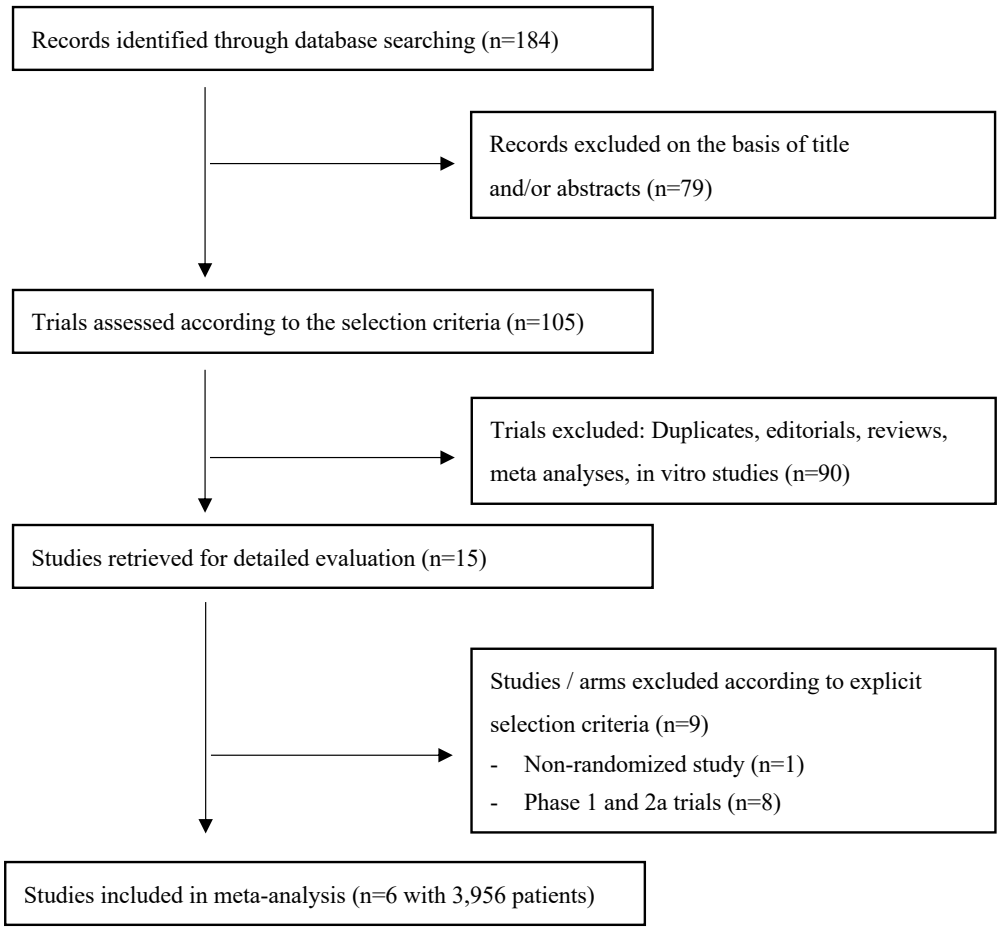

Supplementary Table 1: Risk of bias assessment of all included trials, according to the Cochrane collaboration guidelines.

**Supplementary Table 2 – GRADE assessment of primary outcomes**

| Outcome (No. of studies) | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | Summary of findings | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | No. of subjects BA/placebo | Pooled OR (95% CI) | Certainty rating |
| MACE (4) | RCT | Not serious | Serious[a] | Not serious | Serious[c] | Undetected | 2273/1140 | 0.84 (0.61-1.15) | ⊕⊕○○ Low |
| All-cause mortality (5) | RCT | Not serious | Not serious | Serious[b] | Serious[d] | Undetected | 2642/1253 | 2.37 (0.80-6.99) | ⊕⊕○○ Low |
| Cardiovascular mortality (3) | RCT | Not serious | Not serious | Not serious | Serious[e] | Undetected | 2243/1110 | 1.66 (0.45-6.04) | ⊕⊕⊕○ Moderate |
| Nonfatal myocardial infarction (4) | RCT | Not serious | Not serious | Not serious | Serious[f] | Undetected | 2273/1140 | 0.57 (0.32-0.99) | ⊕⊕⊕○ Moderate |

Supplementary Table 2: The grading of recommendation, assessment, development and evaluation (GRADE) working group assessment of primary outcomes. Ratings: Very low=the true effect is likely to be substantially different from the estimated effect; Low=the true effect may be substantially different from the estimated effect; Moderate=the true effect is likely to be close to the estimated effect; High=very confident that the true effect is close to the estimated effect. [a] Inconsistency of direction of effect; [b] Outcome time frame insufficient; [c] Small number of included studies/pooled estimate not consistent with benefit and harm; [d] Rare event/pooled estimate not consistent with benefit and harm; [e] Rare event/small number of included studies/pooled estimate not consistent with benefit and harm; [f] Small number of included studies. BA=bempedoic acid, CI=confidence interval; MACE=major adverse cardiovascular events; RCT=randomized controlled tiral.

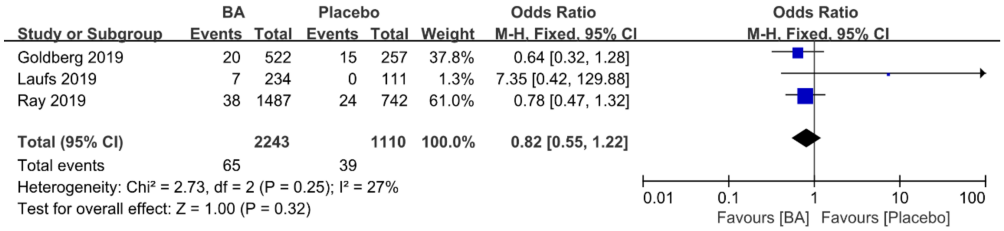
**Supplementary Figure 1 – Summary PRISMA flow-chart of the systematic review process**



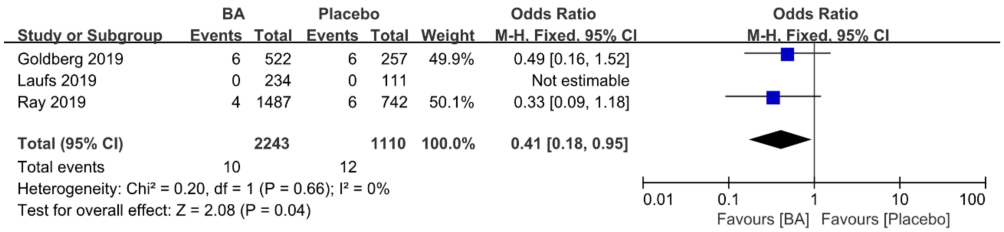

Supplementary Figure 1: PRISMA flow chart summarizing the systematic review process: A total of 184 records identified through database searching were evaluated and reduced to six studies included in quantitative synthesis. RCT=randomized controlled trial.

**Supplementary Figure 2 – Additional efficacy outcomes of BA vs. placebo therapy**

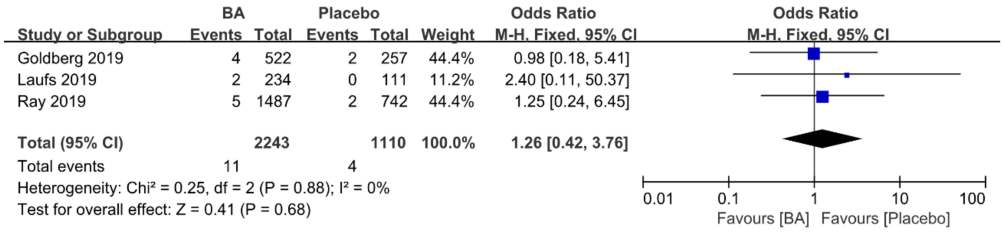
A) Coronary revascularization



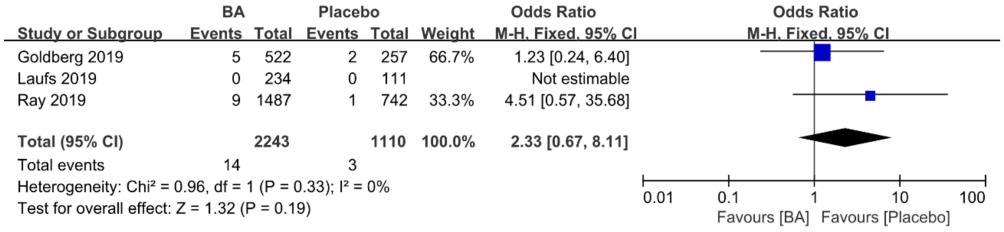

B) Non-coronary revascularization



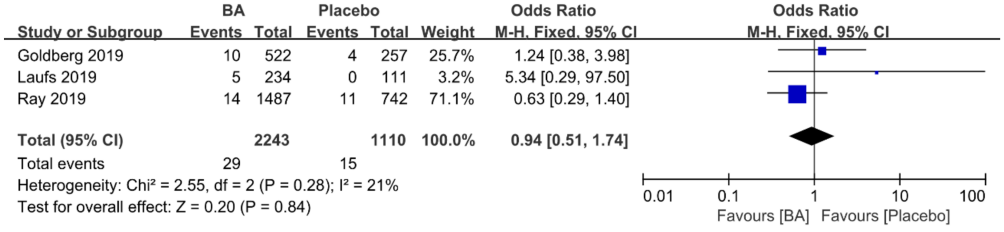

C) Nonfatal stroke




D) Hospitalization for heart failure



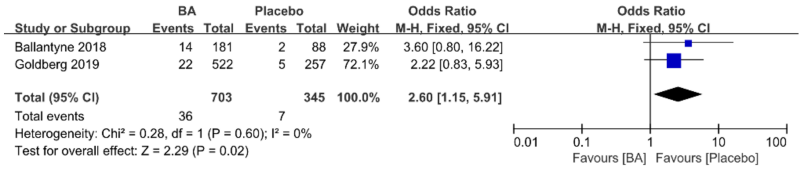

E) Hospitalization for unstable angina



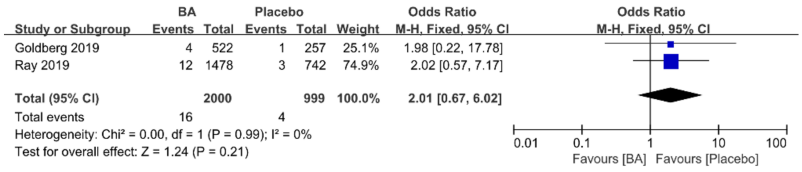

Supplementary Figure 2: Individual and summary odds ratios of additional efficacy outcomes of coronary (A) and non-coronary (B) revascularization, nonfatal stroke (C), hospitalization for heart failure (D) or unstable angina (E) for bempedoic acid vs. placebo therapy. Fixed effects model, Cochran-Mantel-Haenszel-estimates; Tau² and I² are measures of heterogeneity. BA=bempedoic acid; M-H=Mantel-Haenszel.

**Supplementary Figure 3 – Additional safety outcomes of BA vs. placebo therapy**

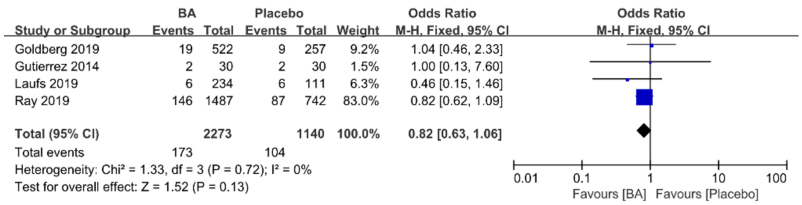
A) Elevation in uric acid



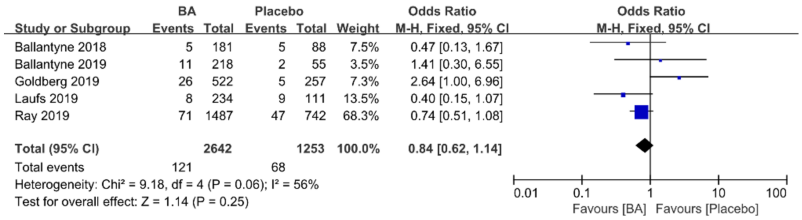

B) Increase in serum creatinine



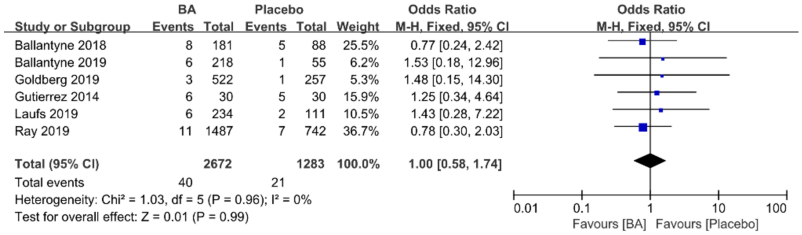

C) Upper respiratory tract infection



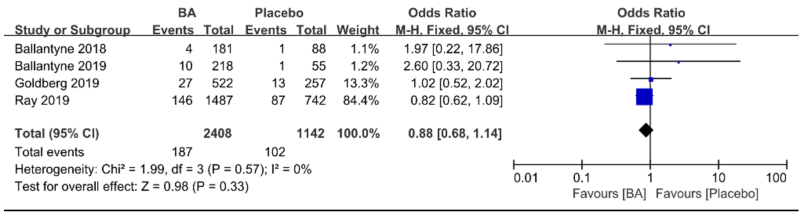

D) Urinary tract infection




E) Neurocognitive disorder



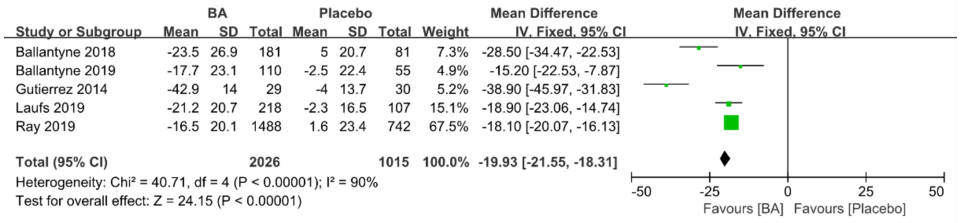

F) Nasopharyngitis



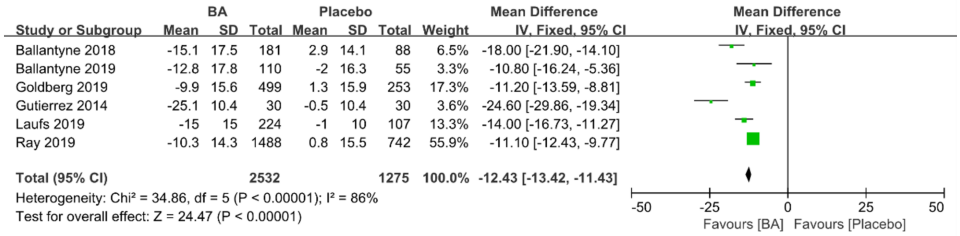

Supplementary Figure 3: Individual and summary odds ratios of additional safety outcomes of elevation in uric acid (A), upper respiratory tract infection (B), urinary tract infection (C), neurocognitive disorder (D), nasopharyngitis (E) and increase in serum creatinine (F) for BA vs. placebo therapy. Fixed effects model, Cochran-Mantel-Haenszel estimates; Tau² and I² are measures of heterogeneity. BA=bempedoic acid; M-H=Mantel-Haenszel.

**Supplementary Figure 4 – Serum lipid levels of BA vs. placebo therapy**

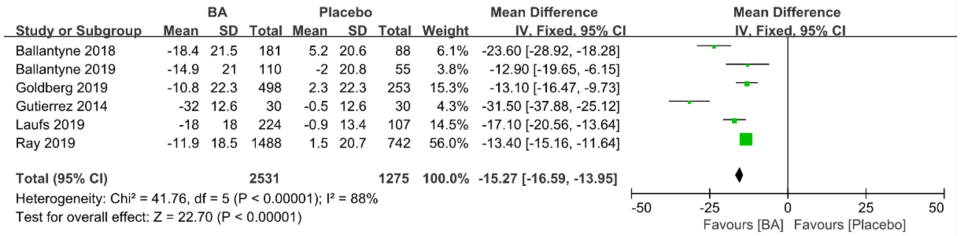
A) LDL-C



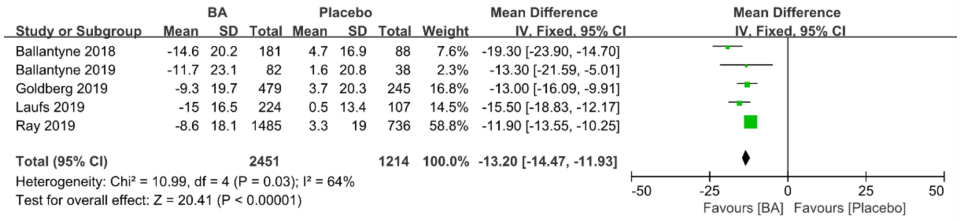

B) Total cholesterol



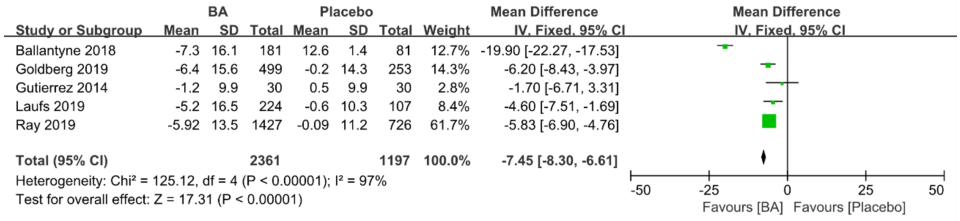

C) Non-HDL-C



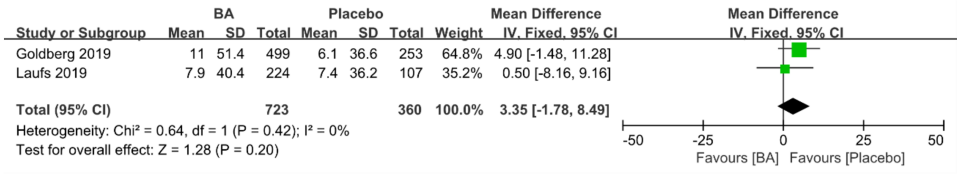

D) Apolipoprotein B




E) HDL-C




F) Trigylcerides




Supplementary Figure 4: Indivual and summary mean differences with 95% confidence intervals (corresponding to Figure 3) of serum lipid levels for bempedoic acid vs. placebo therapy: LDL-C (A), total cholesterol (B), Non-HDL-C (C), Apolipoprotein B (D), HDL-C (E) and triglycerides (F). Fixed effects model, Cochran-Mantel-Haenszel estimates; Tau² and I² are measures of heterogeneity. BA=bempedoic acid; HDL-C=high-density-lipoprotein cholesterol; LDL-C=low-density-lipoprotein cholesterol; M-H=Mantel-Haenszel; non-HDL-C=non-high density lipoprotein cholesterol.