Supplementary File 4: Cochrane risk of bias assessment of the included studies

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| **Author judgment** | **Risk of bias** | **Ballantyne et al. 2016** |
| "Patients were randomized in a 1:1:1 ratio to ETC-1002 120 mg, ETC-1002 180 mg, or matching placebo once daily for 12 weeks in addition to ongoing statin therapy." | Low risk | Random sequence generation (selection bias) |
|  | Unclear risk | Allocation concealment (selection bias) |
| "double-blind" | Low risk | Blinding of participants and personnel (performance bias) |
| "double-blind" | Low risk | Blinding of outcome assessment (detection bias) |
| "Efficacy analyses were performed on the modified intent to- treat (mITT) population." | low risk | Incomplete outcome data (attrition bias) |
| Important safety and efficacy outcomes were reported. | Low risk | Selective reporting (reporting bias) |
| "This study was Financially supported by Esperion Therapeutics, Inc., Ann Arbor, Michigan." | High risk | Other bias |
| **Author judgment** | **Risk of bias** | **Thompson et al. 2016** |
| "Patients were stratified (1:1) by history of statin intolerance and randomized at week 0 in a 4:4:4:1:1 ratio to once-daily treatment with capsules containing ETC-1002 120 mg, ETC-1002 180 mg, EZE, ETC-1002 120 mg plus EZE, or ETC-1002 180 mg plus EZE." | Low risk | Random sequence generation (selection bias) |
|  | Unclear risk | Allocation concealment (selection bias) |
| "double-blind" | Low risk | Blinding of participants and personnel (performance bias) |
| " double-blind" | Low risk | Blinding of outcome assessment (detection bias) |
| ITT analysis was performed | Low risk | Incomplete outcome data (attrition bias) |
| All pre-specified outcomes were reported. | Low risk | Selective reporting (reporting bias) |
| "The design, study conduct, analysis, and financial support of this clinical trial were provided by Esperion Therapeutics, Inc." | High risk | Other bias |
| **Author judgment** | **Risk of bias** | **Thompson et al. 2015** |
| "Patients were randomized in a 2:1 ratio to receive either oral ETC-1002 or placebo daily for 8 weeks." | Low risk | Random sequence generation (selection bias) |
|  | Unclear risk | Allocation concealment (selection bias) |
| "double-blind" | Low risk | Blinding of participants and personnel (performance bias) |
| "double-blind" | Low risk | Blinding of outcome assessment (detection bias) |
| ITT analysis was performed | Low risk | Incomplete outcome data (attrition bias) |
| All pre-specified outcomes were reported. | Low risk | Selective reporting (reporting bias) |
| "This clinical trial was funded by Esperion Therapeutics, Inc." | High risk | Other bias |
| **Author judgment** | **Risk of bias** | **Gutierrez et al. 2014** |
| "Patients randomized to receive ETC-1002 80 mg QD for 2 weeks followed by 120 mg QD for 2 weeks or placebo for 4 weeks." | Low risk | Random sequence generation (selection bias) |
|  | Unclear risk | Allocation concealment (selection bias) |
| " double-blind " | Low risk | Blinding of participants and personnel (performance bias) |
| " double-blind " | Low risk | Blinding of outcome assessment (detection bias) |
| Patient discontinued treatment owing to an adverse event. | High risk | Incomplete outcome data (attrition bias) |
| All pre-specified outcomes were reported. | Low risk | Selective reporting (reporting bias) |
| "This trial was funded by Esperion Therapeutics, Inc." | High risk | Other bias |
| **Author judgment** | **Risk of bias** | **Ballantyne et al. 2013** |
| "patients randomized to receive(1:1:1:1), ETC-1002 40, 80, or 120 mg or matching placebo once daily for 12 weeks". | Unclear risk | Random sequence generation (selection bias) |
|  | Unclear risk | Allocation concealment (selection bias) |
| "double-blind" | Low risk | Blinding of participants and personnel (performance bias) |
| "double-blind" | Low risk | Blinding of outcome assessment (detection bias) |
| Patient discontinued treatment owing to an adverse event. | High risk | Incomplete outcome data (attrition bias) |
| All pre-specified outcomes were reported. | Low risk | Selective reporting (reporting bias) |
| "This trial was funded by Esperion Therapeutics, Inc." | High risk | Other bias |

The risk of performance, detection, and attrition bias were assessed on the outcome level and a general verdict was entitled for the entire study when all outcomes had a similar nature of assessment and no exceptions were mentioned in the study that indicate a possible risk of bias in a specific outcome.