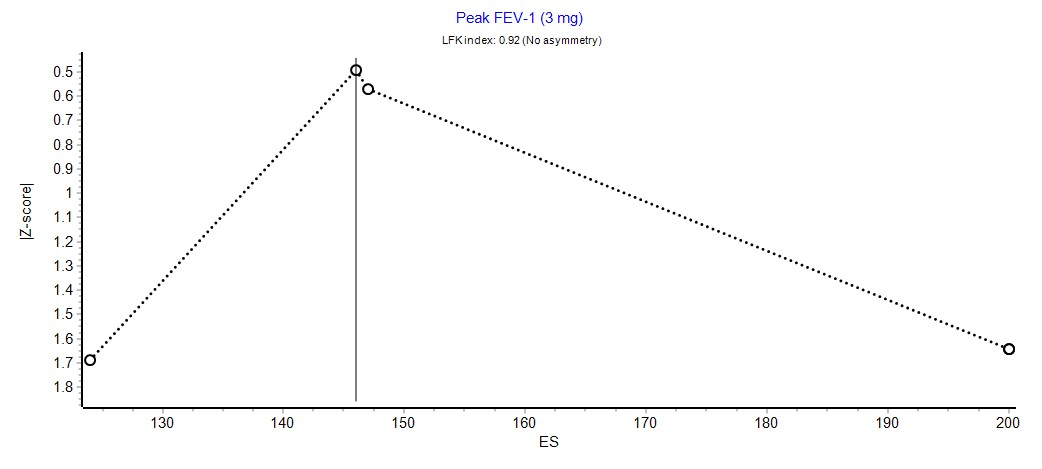
**Supplementary Material**

**Efficacy and Safety of Ensifentrine, A Novel Phosphodiesterase 3 and 4 Inhibitor, in Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis**

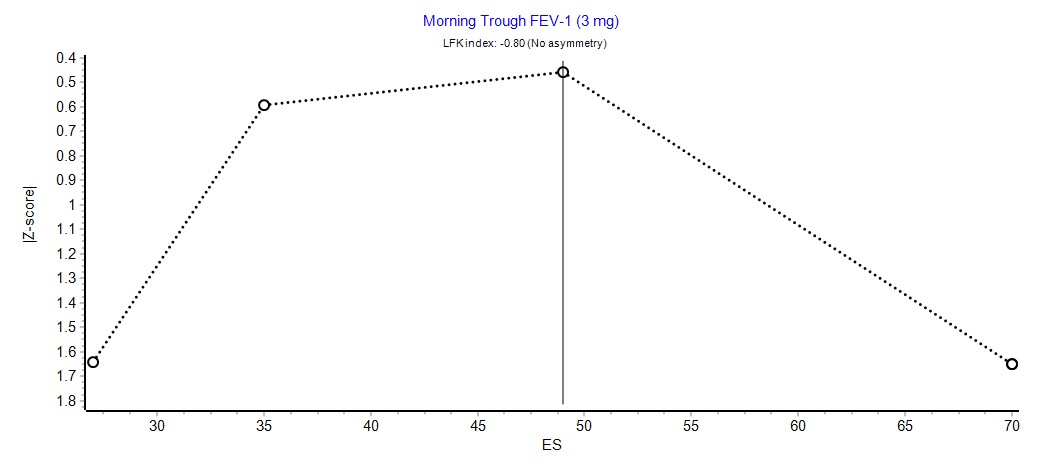
This supplemental material has been provided by the authors to give readers additional information about their work.

**Supplementary Table S1:** Detailed Database Search Strategy

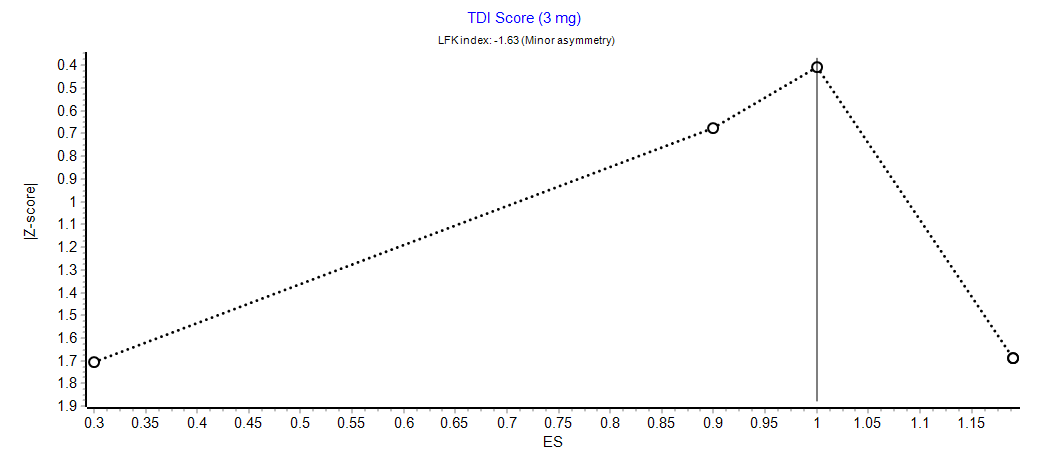
| **Database** | **Search String** |
| --- | --- |
| PubMed, MEDLINE  (42 Results) | (("ensifentrine" OR “RPL554” OR “dual phosphodiesterase 3 and 4 Inhibitor” OR “PDE3/4 inhibitor”) AND ("pulmonary disease, chronic obstructive"[MeSH Terms] OR ("pulmonary"[All Fields] AND "disease"[All Fields] AND "chronic"[All Fields] AND "obstructive"[All Fields]) OR "chronic obstructive pulmonary disease"[All Fields] OR ("chronic"[All Fields] AND "obstructive"[All Fields] AND "pulmonary"[All Fields] AND "disease"[All Fields]) OR "COPD"[All Fields]) AND ("efficacies"[All Fields] OR "efficacious"[All Fields] OR "efficaciously"[All Fields] OR "efficaciousness"[All Fields] OR "efficacy"[All Fields] OR ("effect"[All Fields] OR "effecting"[All Fields] OR "effective"[All Fields] OR "effectively"[All Fields] OR "effectiveness"[All Fields] OR "effectivenesses"[All Fields] OR "effectives"[All Fields] OR "effectivities"[All Fields] OR "effectivity"[All Fields] OR "effects"[All Fields])) |
| Scopus  (33 results) | copd OR "chronic obstructive pulmonary disease" OR chronic AND obstructive AND pulmonary AND disease OR obstructive AND pulmonary AND disease |
| Google Scholar  (89 results) | ensifentrine AND COPD AND RPL554 AND "Chronic obstructive pulmonary disease" |
| Cochrane Library  (43 results) | (ensifentrine OR RPL554) AND (COPD OR Chronic obstructive pulmonary disease) |



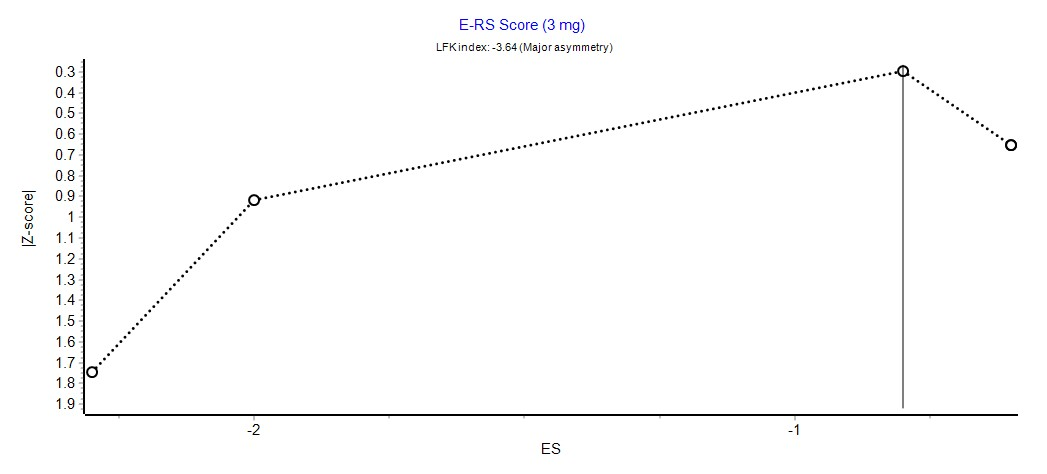
**Supplementary Figure F1:** Doi plot for pooled Peak FEV-1 for (Ensifentrine 3 mg dosage)



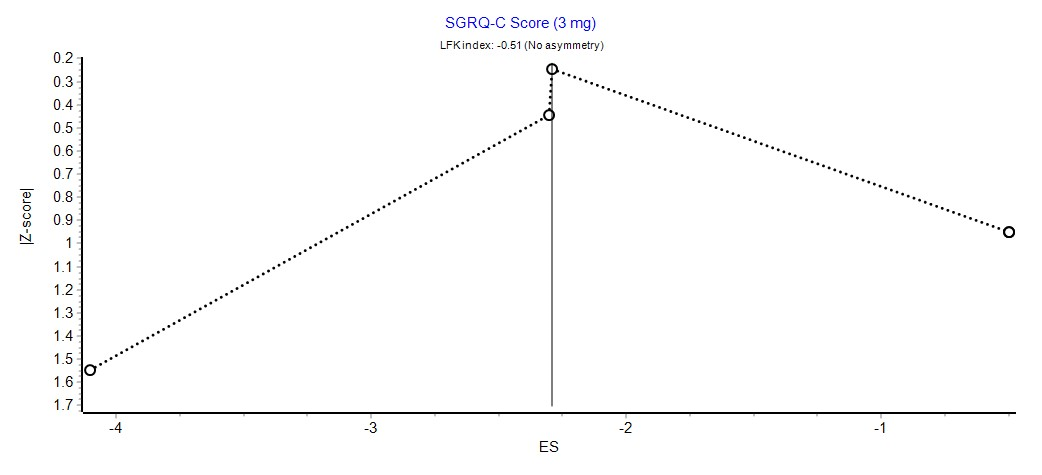
**Supplementary Figure F2:** Doi plot for pooled Morning Trough FEV-1 for (Ensifentrine 3 mg dosage)

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**Supplementary Figure F3:** Doi plot for pooled TDI Score (Ensifentrine 3 mg dosage)

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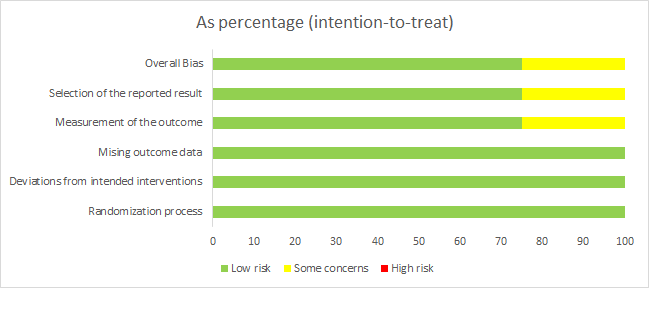
**Supplementary Figure F4:** Doi plot for pooled E-RS Score for (Ensifentrine 3 mg dosage)



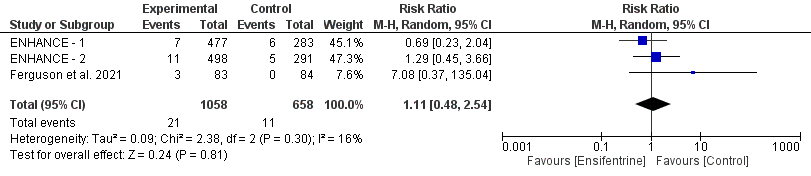
**Supplementary Figure F5:** Doi plot for pooled SGRQ-C Score for (Ensifentrine 3 mg dosage)



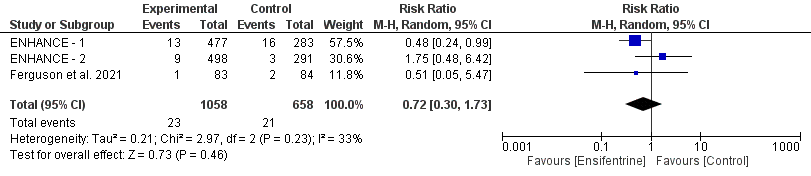
**Supplementary Figure F6:** Traffic light plot showing risk of bias assessment



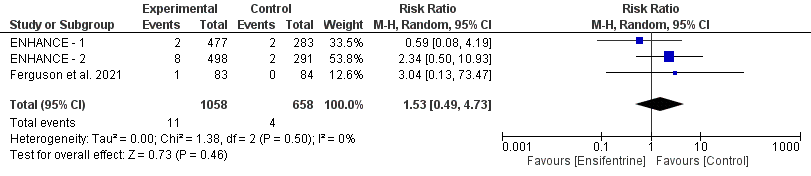
**Supplementary Figure F7:** Summary plot showing risk of bias assessment



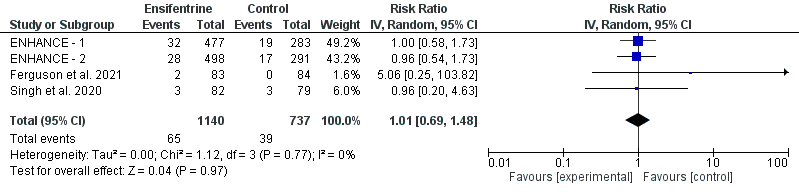
**Supplementary Figure F8:** Pooled risk ratios for worsening of COPD symptoms reported as an adverse events for 3 mg dose



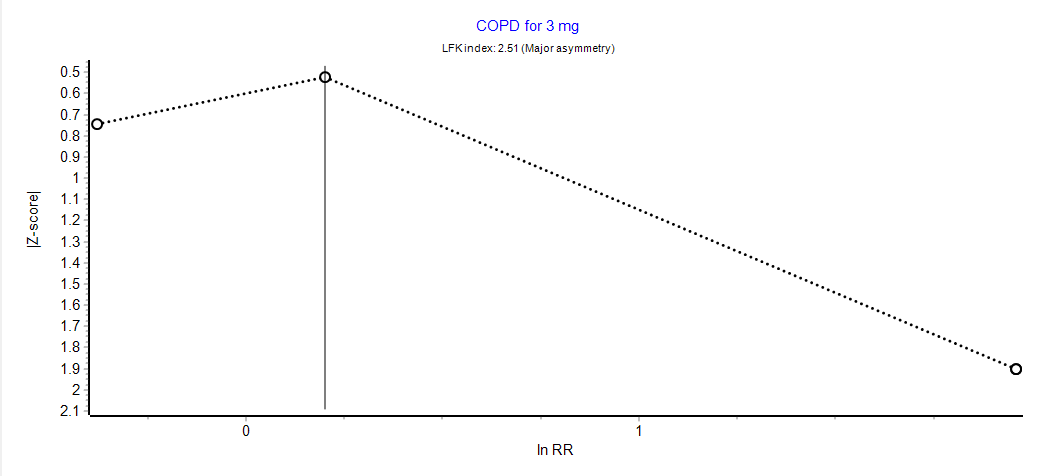
**Supplementary Figure F9:** Pooled risk ratios for hypertension reported as an adverse event for 3 mg dose



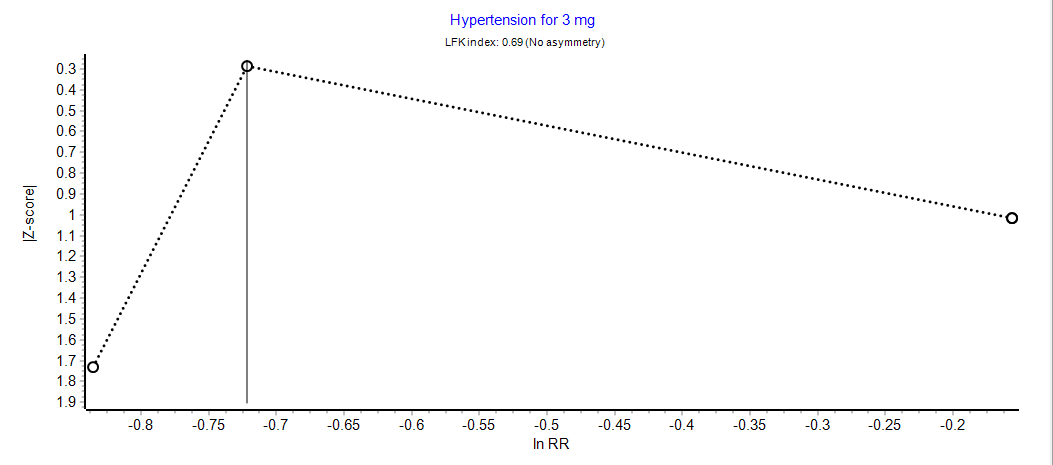
**Supplementary Figure F10:** Pooled risk ratios for diarrhea reported as an adverse event for 3 mg dose



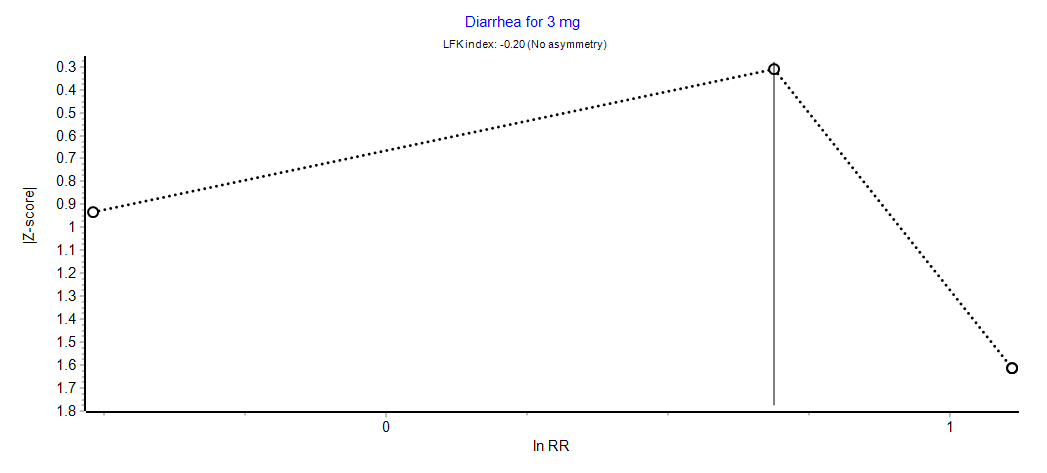
**Supplementary Figure F11:** Pooled risk ratios for serious adverse events reported as for 3 mg dose



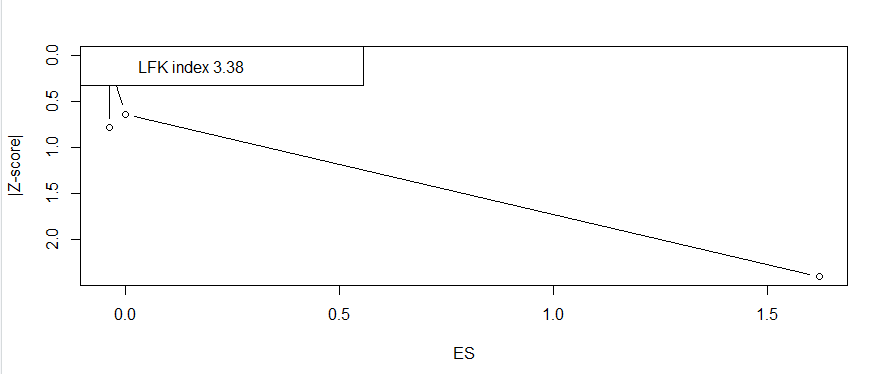
**Supplementary Figure F12:** Doi plot for pooled worsening of COPD symptoms reported as an adverse event for 3 mg dose



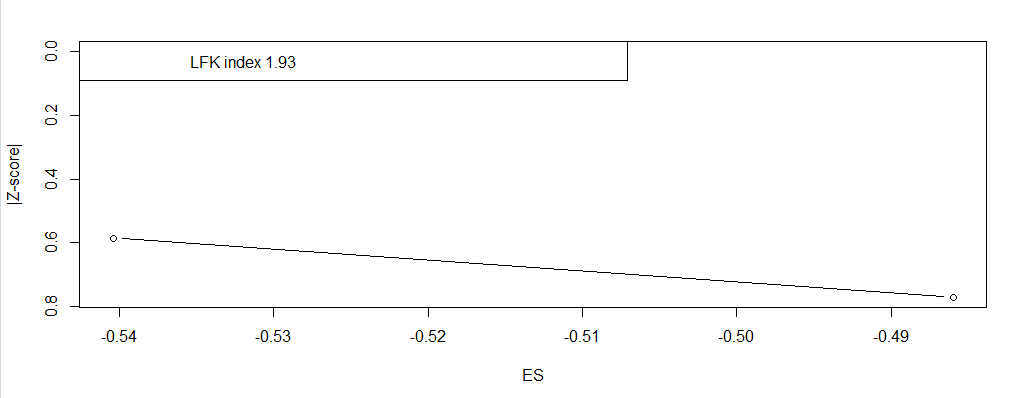
**Supplementary Figure F13:** Doi plot for pooled hypertension reported as an adverse event for 3 mg dose

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**Supplementary Figure F14:** Doi plot for pooled diarrhea reported as an adverse event for 3 mg dose



**Supplementary Figure F15:** Doi plot for pooled serious adverse events for 3 mg dose



**Supplementary Figure F16:** Doi plot for pooled COPD Exacerbation for the 3 mg dose