### Supplementary Table S1 Search strategies

<table>
<thead>
<tr>
<th>Database</th>
<th>Dates searched</th>
<th>Search terms</th>
<th>Results found</th>
</tr>
</thead>
</table>
| MEDLINE  (source, PubMed) | 1966–July 2018 | #1: Thrombomodulin [MeSH]: 2411  
#2: Recomodulin: 11  
#3: ART-123: 28  
#4: #1 OR #2 OR #3: 2420  
#5: Sepsis [MeSH]: 111676  
#6: “Systemic Inflammatory Response Syndrome” [Mesh]: 115268  
#7: “Multiple Organ Failure” [Mesh]: 10046  
#8: “Disseminated Intravascular Coagulation” [Mesh]: 10657  
#9: #5 OR #6 OR #7 OR #8: 131238  
#11: #4 AND #9 AND #10: 162 | 162 |
| Cochrane Central Register of Controlled Trials | July 2018 | #1: MeSH descriptor: [Thrombomodulin] explode all trees: 91  
#2: Recomodulin: ti,ab,kw: 1  
#3: ART-123: ti,ab,kw: 24  
#4: #1 OR #2 OR #3: 113  
#5: MeSH descriptor: [Sepsis] explode all trees: 4266  
#6: MeSH descriptor: [Systemic Inflammatory Response Syndrome] explode all trees: 4592  
#7: MeSH descriptor: [Multiple Organ Failure] explode all trees: 397  
#8: MeSH descriptor: [Disseminated Intravascular Coagulation] explode all trees: 107  
#9: #5 OR #6 OR #7 OR #8: 4899  
#10: #4 AND #9: 25 | 25 |
#2: recomodulin: 42  
#3: ART-123: 115  
#4: #1 OR #2 OR #3: 6509  
#5: 'sepsis'/exp: 240308  
#6: 'systemic inflammatory response syndrome'/exp: 246330  
#7: 'multiple organ failure'/exp: 33880  
#8: 'disseminated intravascular clotting'/exp: 23261  
#9: #5 OR #6 OR #7 OR #8: 285779  
#10: ‘crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR (random’ OR factorial’ OR crossover’ OR cross NEXT/1 over’ OR placebo’ OR double’ NEAR/1 blind’ OR single’ NEAR/1 blind’ OR assign’ OR allocat’ OR volunteer’):de,ab,ti: 2276378  
#11: #4 AND #9 AND #10: 574 | 168 |
| ICHUSHI Web<sup>a</sup> | 1983–July 2018 | #1: Thrombomodulin/TH OR Thrombomodulin/AL: 3766  
#2: “Thrombomodulin Alfa”/TH OR Recomodulin/AL: 1226  
#3: ART-123/AL: 16  
#4: #1 OR #2 OR #3: 3770  
#5: Sepsis/TH OR “septic shock”/TH: 37453  
#6: “Systemic inflammatory response syndrome”/TH: 40023  
#7: “Multiple Organ Failure”/TH: 7150  
#8: “Disseminated intravascular coagulation”/TH: 13613  
#9: #5 OR #6 OR #7 OR #8: 56862  
#10: #4 AND #9, RD = (MA,RCT,CCT,CS): 65 | 65 |

<sup>a</sup>Search terms in Japanese characters were also used in the search.
Supplementary Fig. S1 Risk of bias graph: review authors’ judgements about each risk of bias item presented as percentages across all included studies.

Supplementary Fig. S2 Funnel plot of comparison: rhTM versus control: all-cause mortality at 28-days.

Supplementary Fig. S3 Forest plot of the comparison: rhTM versus control: all-cause mortality at 28 days, sub-group analysis by risk-of-bias in each trial. Abbreviations: CI, confidence interval; M-H, Mantel-Haenszel; rhTM, recombinant human thrombomodulin; RoB, risk of bias.
Supplementary Fig. S4 Forest plot of the comparison: rhTM versus control: all-cause mortality at 28 days, sub-group analysis by studied country, sample size, and used DIC criteria. Abbreviations: CI, confidence interval; M-H, Mantel-Haenszel; rhTM, recombinant human thrombomodulin.

Supplementary Fig. S5 Forest plot of the comparison: rhTM versus control: all-cause mortality at 28 days, sub-group analysis by baseline disease severity indicated by the control event rate. Abbreviations: CI, confidence interval; M-H, Mantel-Haenszel; rhTM, recombinant human thrombomodulin.