

1.2 All-cause mortality (21-29 days) [critical]

Study or Subgroup	Sarilumab		Standard care		Total	Weight	Risk Ratio		Risk Ratio M-H, Random, 95% CI	Risk of Bias
	Events	Total	Events	Total			M-H, Random, 95% CI	A B C D E F G		
Lescure 2021 [critical]	18	133	6	29	7.6%	0.65	[0.28, 1.50]			
REMAP-CAP sarilumab	10	45	142	397	15.9%	0.62	[0.35, 1.09]			
Sivapalasingam 2021 crit	243	758	74	214	76.5%	0.93	[0.75, 1.15]			
Total (95% CI)	271	936	222	640	100.0%	0.85	[0.67, 1.07]			

Total events: 271 (Sarilumab), 222 (Standard care)
 Heterogeneity: Tau² = 0.01; Chi² = 2.21, df = 2 (P = 0.33); I² = 10%
 Test for overall effect: Z = 1.39 (P = 0.16)

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

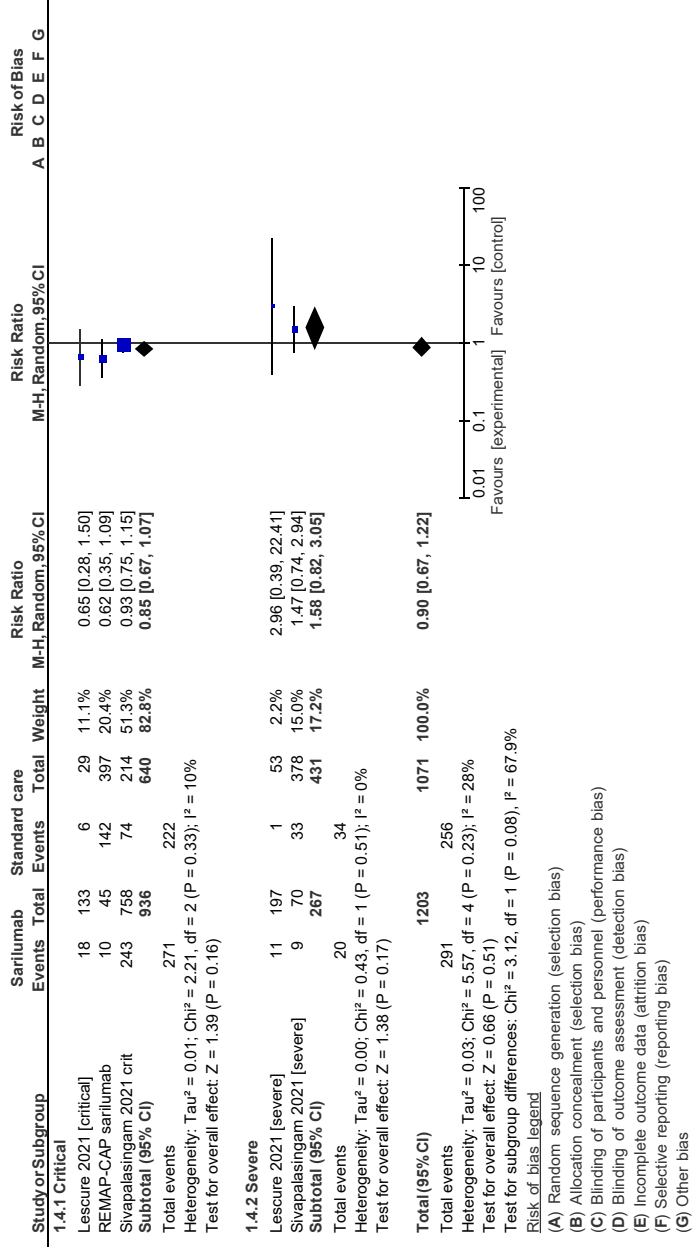
1.3 All-cause mortality (21-29 days) [severe]

Study or Subgroup	Sarilumab		Standard care		Total	Weight	Risk Ratio		Risk Ratio		Risk of Bias							
	Events	Total	Events	Total			M-H, Random, 95% CI	M-H, Random, 95% CI	A	B	C	D	E	F	G			
Lescure 2021 [severe]	11	197	1	53	53	10.4%	2.96	[0.39, 22.41]										
Sivapalasingam 2021 [severe]	9	70	33	378	378	89.6%	1.47	[0.74, 2.94]										
Total (95% CI)		267		431	431	100.0%	1.58	[0.82, 3.05]										
Total events	20		34															
Heterogeneity: $\tau^2 = 0.00$; $\text{Chi}^2 = 0.43$, $\text{df} = 1$ ($P = 0.51$); $I^2 = 0\%$																		
Test for overall effect: $Z = 1.38$ ($P = 0.17$)																		



Risk of bias legend
 (A) Random sequence generation (selection bias)
 (B) Allocation concealment (selection bias)
 (C) Blinding of participants and personnel (performance bias)
 (D) Blinding of outcome assessment (detection bias)
 (E) Incomplete outcome data (attrition bias)
 (F) Selective reporting (reporting bias)
 (G) Other bias

1.4 All-cause mortality (21-29 days) [subgroups]



1.5 Adverse events

Study or Subgroup	Sarilumab		Standard care		Total	Weight	Risk Ratio		Risk of Bias							
	Events	Total	Events	Total			M-H, Random, 95% CI	M-H, Random, 95% CI		A	B	C	D	E	F	G
Hermine 2022	32	48	22	33	33	9.1%	1.00	[0.73, 1.37]	+	+	+	+	+	+	+	+
Lescure 2021	224	332	55	84	84	30.0%	1.03	[0.87, 1.22]	+	+	+	+	+	+	+	+
Sivapalasingam 2021	642	1140	157	309	309	60.9%	1.11	[0.98, 1.25]	+	+	+	+	+	+	+	+
Total (95% CI)	1520		426		426	100.0%	1.07	[0.98, 1.18]								
Total events	898		234													

Heterogeneity: Tau² = 0.00; Chi² = 0.70, df = 2 (P = 0.70); I² = 0%
 Test for overall effect: Z = 1.49 (P = 0.14)

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

1.6 Clinical improvement (day 22)

Study or Subgroup	Sarilumab		Standard care		Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
	Events	Total	Events	Total			
Sivapalasingam 2021	510	857	146	240	100.0%	0.98 [0.87, 1.10]	
Total (95% CI)	510	857	146	240	100.0%	0.98 [0.87, 1.10]	

Total events: 510 (Sarilumab), 146 (Standard care)
 Heterogeneity: Not applicable
 Test for overall effect: Z = 0.37 (P = 0.71)

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

1.7 Time to improvement (median)

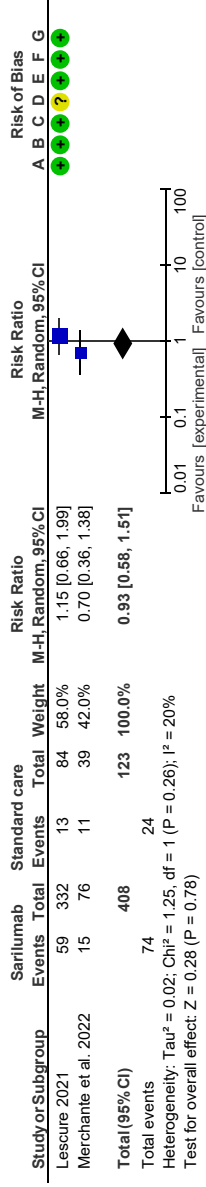
Study or Subgroup	Sarilumab		Standard care		Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
	Mean	SD	Mean	SD			
Total (95% CI)	0	0	0	0	Not estimable	Not estimable	

Heterogeneity: Not applicable
 Test for overall effect: Not applicable

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

1.8 Requiring ventilation (HFNO, NIV, MV)



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

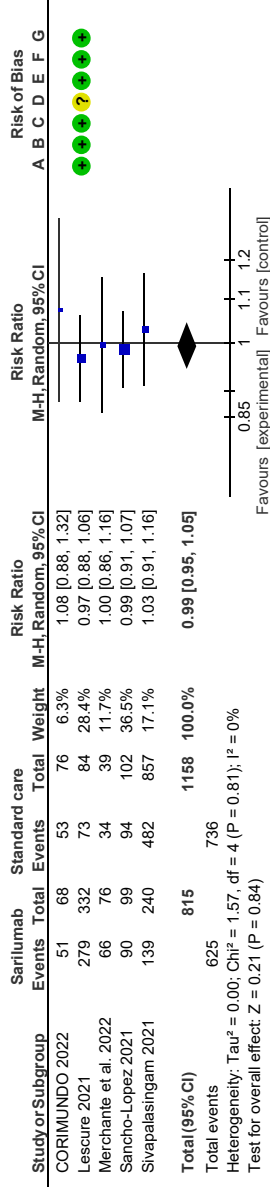
1.9 Admission to ICU

Study or Subgroup	Sarilumab		Standard care		Total	Weight	Risk Ratio		Risk Ratio M-H,Random,95%CI	Risk of Bias
	Events	Total	Events	Total			M-H,Random,95%CI	A B C D E F G		
Lescure 2021	28	212	7	56	56	58.8%	1.06	[0.49, 2.29]	■	●●●●●●●
Sancho-Lopez 2021	7	99	10	102	102	41.2%	0.72	[0.29, 1.82]	■	●●●●●●●
Total(95%CI)	311	311	158	158	158	100.0%	0.90	[0.50, 1.63]	◆	●●●●●●●
Total events	35		17							
Heterogeneity: $\tau^2 = 0.00$; $\text{Chi}^2 = 0.39$, $\text{df} = 1$ ($P = 0.53$); $I^2 = 0\%$										
Test for overall effect: $Z = 0.34$ ($P = 0.74$)										

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

1.10 Discharged from hospital (end of follow-up)



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

1.11 Clinical recovery (day 22)

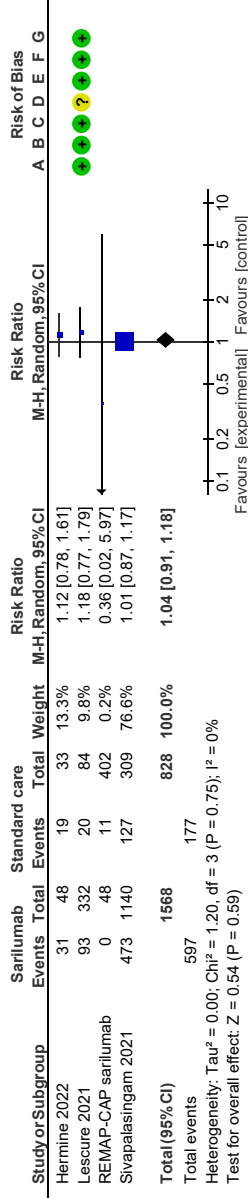
Study or Subgroup	Sarilumab		Standard care		Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias								
	Events	Total	Events	Total					A	B	C	D	E	F	G		
Sivapalasingam 2021	665	1140	182	309	309	100.0%	0.99 [0.89, 1.10]	0.99 [0.89, 1.10]									
Total (95% CI)		1140		309	309	100.0%	0.99 [0.89, 1.10]	0.99 [0.89, 1.10]									
Total events	665		182														
Heterogeneity: Not applicable																	
Test for overall effect: Z = 0.18 (P = 0.86)																	

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias



1.12 Serious adverse events



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

1.13 Mechanical ventilation

Study or Subgroup	Sarilumab		Standard care		Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias			
	Events	Total	Events	Total						A	B	C
Merchante et al. 2022	9	76	4	39	100.0%	1.15 [0.38, 3.51]						
Total (95% CI)		76		39	100.0%	1.15 [0.38, 3.51]						
Total events: 9												
Heterogeneity: Not applicable												
Test for overall effect: Z = 0.25 (P = 0.80)												

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias



1.14 Respiratory failure

Study or Subgroup	Sarilumab		Standard care		Total Weight	Risk Ratio M-H,Random,95%CI	Risk Ratio M-H,Random,95%CI	Risk of Bias		
	Events	Total	Events	Total					A	B
Sancho-Lopez 2021	16	99	16	102	100.0%	1.03 [0.55, 1.94]	1.03 [0.55, 1.94]			
Total (95% CI)	16	99	16	102	100.0%	1.03 [0.55, 1.94]	1.03 [0.55, 1.94]			

Total events: 16

Heterogeneity: Not applicable

Test for overall effect: Z = 0.09 (P = 0.93)

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias