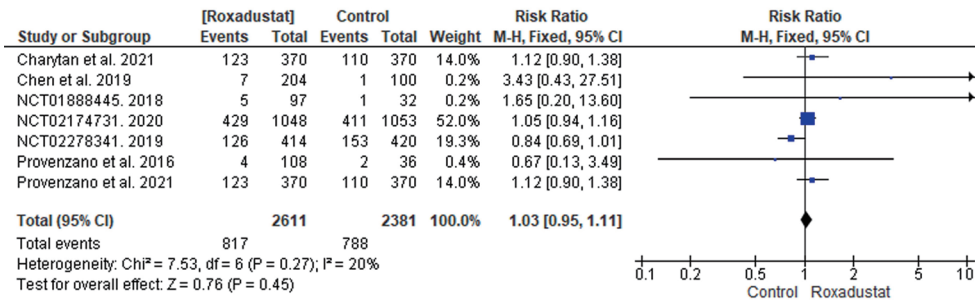**Figure S1** Forest plot of the Subgroup analysis.

Figure S2 Forest plot of comparison: 2 Adverse effects, outcome: 2.4 Cardiovascular adverse effects.
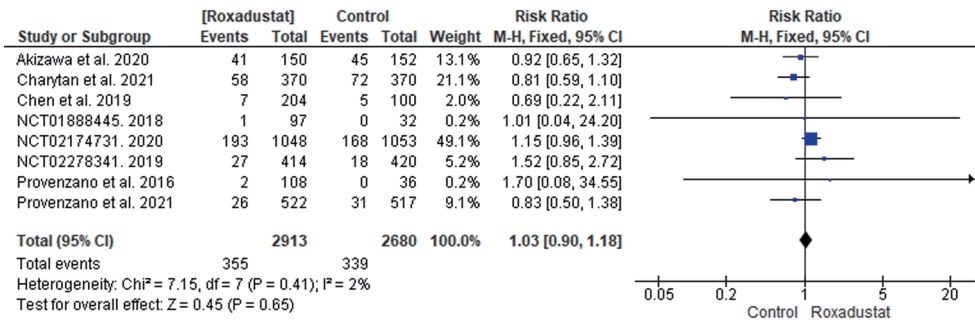

Figure S3 Forest plot of comparison: 2 Adverse effects, outcome: 2.5 Injury, poisoning, and procedural complications.
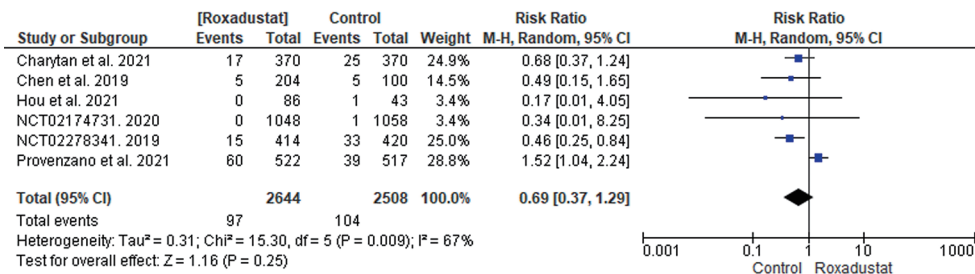

Figure S4 Forest plot of comparison: 2 Adverse effects, outcome: 2.6 Muscle spasm.
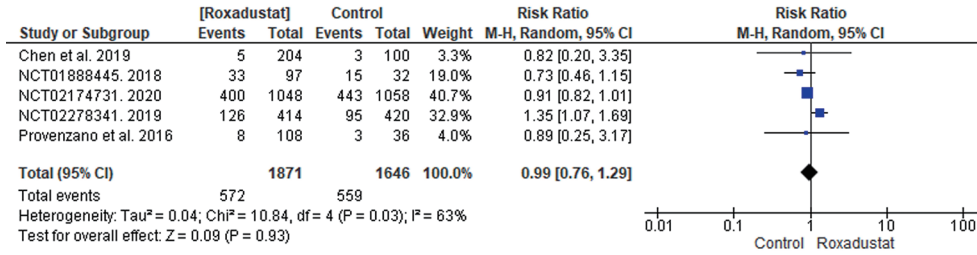
Figure S5 Forest plot of comparison: 2 Adverse effects, outcome: 2.7 Infection or infestation.
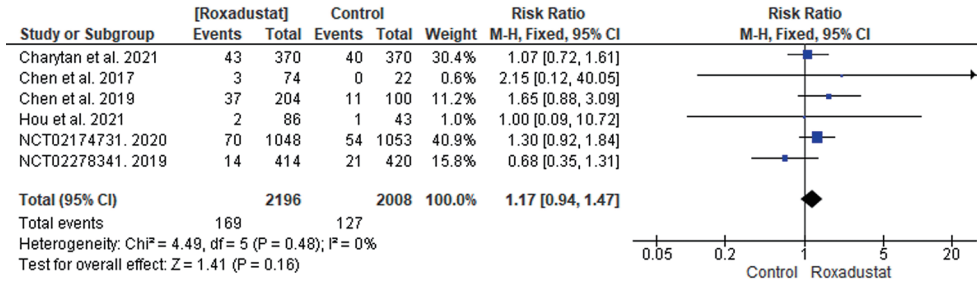

Figure S6 Forest plot of comparison: 2 Adverse effects, outcome: 2.8 Upper respiratory tract infections.
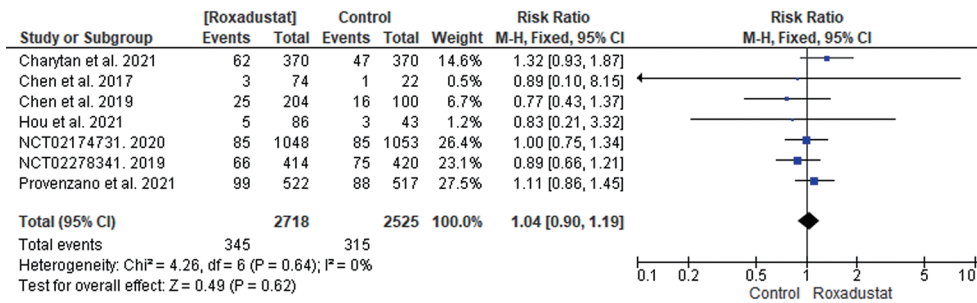

Figure S7 Forest plot of comparison: 2 Adverse effects, outcome: 2.9 Hypertension.
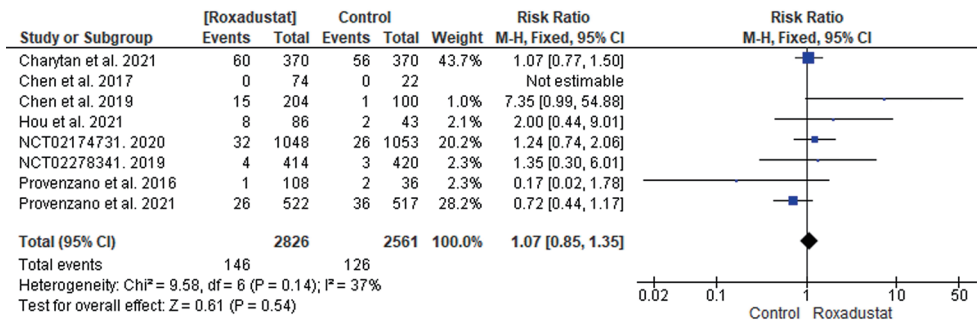

Figure 8 Forest plot of comparison: 2 Adverse effects, outcome: 2.10 Hyperkalemia.

Table S1 Search terms and results in different databases

Database name	Search terms	Search fields	Result
PubMed	(Roxadustat OR ASP1517 OR FG4592 OR "FG-4592") AND (kidney OR renal) AND (Anemia)	All Field	104
Web Of Science	(Roxadustat OR ASP1517 OR FG4592 OR "FG-4592") AND (kidney OR renal) AND (Anemia)	Topic	150
Scopus	(Roxadustat OR ASP1517 OR FG4592 OR "FG-4592") AND (kidney OR renal) AND (Anemia)	Title, Abstract, Keywords	159
Cochrane	((Roxadustat) OR (ASP1517) OR (FG4592) OR (FG-4592)) AND ((kidney) OR (renal)) AND ((Anemia))	Title, Abstract Keyword	113
Embase	(roxadustat OR asp1517 OR fg4592 OR 'fg 4592') AND (kidney OR renal) AND anemia	All Field	256
Google Scholar	with all of the words: Roxadustat OR FG4592 OR "FG-4592" with at least one of the words: kidney anemia In the title of the article		126

Table S2 The baseline laboratory values of the included patients

Study	Group	Hb level (g/dL), Mean ± SD	TSAT (%), Mean ± SD	Ferritin (ng/mL), Mean ± SD	Hepcidin (ng/mL), Mean ± SD	TIBC (µg/dL), Mean ± SD
Charytan et al. 2021	Roxadustat	10.30 ± 0.66	33.60 ± 10.10	1002.02 ± 459.68	272.85 ± 129.70	201.88 ± 33.56
	Epoetin alfa	10.31 ± 0.66	33.65 ± 9.86	959.24 ± 414.30	270.67 ± 134.52	202.89 ± 36.81
Chen et al. 2017	Roxadustat	10.8 ± 0.7	31.6 ± 16.7	450.5 ± 368.2	176.3 ± 120	217.3 ± 49.6
	rhEPO	10.6 ± 61.0	34.1 ± 14.6	458 ± 361	209.0 ± 127.1	214 ± 38
Chen et al. 2019	Roxadustat	10.4 ± 0.7	33.8 ± 16.6	498.5 ± 487.4	NR	264.7 ± 63.7
	Epoetin alfa	10.5 ± 0.7	30.0 ± 13.8	420.1 ± 406.8	NR	269.7 ± 50.3
Provenzano et al. 2016	Roxadustat	11.2 ± 0.7	29.2 ± 10.0	827.7 ± 474.3	327.1 ± 178.8	199.7 ± 34.0
	Epoetin alfa	11.2 ± 1.0	28.1 ± 14.4	1065.8 ± 657.2	298.7 ± 123.1	202.1 ± 26.7
Provenzano et al. 2021	Roxadustat	8.4 ± 1.0	27.02 ± 9.27	441.38 ± 337.02	173.21 ± 120.21	241.04 ± 43.00
	Epoetin alfa	8.5 ± 1.0	27.55 ± 8.90	436.65 ± 311.67	169.91 ± 127.98	238.06 ± 37.04
NCT02278341	Roxadustat	10.75 ± 0.62	NR	NR	NR	NR
	ESA	10.77 ± 0.62	NR	NR	NR	NR
Hou et al. 2021	Roxadustat	9.0 ± 1.4	31.3 ± 14.2	268.8 ± 297.2	142.8 ± 112.5	237.3 ± 65.3
	ESA	9.0 ± 1.2	29.6 ± 13.2	257.4 ± 190.8	122.0 ± 82.2	230.6 ± 83.2
Nct01888445	Roxadustat	8.84 ± 0.47	43.66 ± 16.01	190.20 ± 187.67	NR	226.2 ± 35.2
	DA	8.8 ± 0.51	37.26 ± 16.06	156.99 ± 102.49	NR	234.5 ± 32.9
Nct02174731	Roxadustat	NR	NR	NR	NR	NR
	Epoetin alfa	NR	NR	NR	NR	NR
Akizawa et al. 2020	Roxadustat	11.02 ± 0.56	28.28 ± 11.70	102.31 ± 83.45	26.44 ± 21.50	242.4 ± 39.1
	DA	11.01 ± 0.60	29.04 ± 10.18	96.28 ± 75.14	24.44 ± 20.99	242.9 ± 34.6

DA, Darbepoetin Alfa; rhEPO, recombinant human erythropoietin; ESA, erythropoiesis-stimulating agent; Hb, hemoglobin; SD, standard deviation; TIBC, total iron-binding capacity; TSAT, transferrin saturation; NR, not reported.

Table S3 The studies assessed C-reactive protein

Study	Group	CRP, Number of patients (%)	
		≤ULN	>ULN
Charytan *et al.* 2021	Roxadustat	178 (48.1%)	189 (51.1%)
	Epoetin alfa	192 (51.8%)	177 (47.7%)
Chen *et al.* 2019	Roxadustat	158 (77.5%)	46 (22.5%)
	Epoetin alfa	80 (80.0%)	20 (20.0%)
Provenzano *et al.* 2021	Roxadustat	289 (55.4%)	228 (43.7%)
	Epoetin alfa	289 (55.5%)	226 (43.4%)
Hou *et al.* 2021	Roxadustat	48 (56%)	38 (44%)
	ESA	25 (58%)	18 (42%)
Akizawa *et al.* 2020	Roxadustat	<ULN, 136 (90.7%) ≥ULN, 14 (9.3%)	
	DA	<ULN, 129 (85.4%) ≥ULN, 22 (14.6%)	

DA, Darbepoetin Alfa; ESA, erythropoiesis-stimulating agent; CRP, C-reactive protein; ULN, upper limit of normal.

Table S4 Publication bias using Egger's regression

Outcome	Intercept	Standard error	Lower limit	Upper limit	t-value	P-value
Hemoglobin	1.26	1.89	-3.09	5.62	0.669	0.523
Ferritin	1.629	1.3211	-1.604	4.86	1.233	0.264
TSAT	1.382	0.7	-0.33	3.1	3.1	0.1
Hepcidin	-0.43	1.4	-3.84	2.99	0.306	0.77
TIBC	-0.95	1.82	-5.63	3.74	0.52	0.63
Serum Iron	0.63	0.9	-1.68	2.94	0.7	0.52
Transferrin	2.46	0.574	-4.833	9.76	4.29	0.146
TEAEs	0.6	0.87	-0.141	2.603	0.689	0.511
Serious TEAEs	0.985	0.421	-0.01	1.98	2.341	0.052

TSAT, transferrin saturation; TIBC, total iron-binding capacity; TEAEs, treatment-emergent adverse effects

Table S5 Meta-analysis of the primary outcomes and sensitivity analysis

Outcome	No. of participants Roxadustat/Control)	No. of trials	Quantitative data synthesis				Heterogeneity analysis		
			SMD	95% CI	Z value	P value	df	P value	I^2 (%)
Hemoglobin level									
All studies	2896/2673	10	0.21	[0.02, 0.39]	2.22	0.03	9	0.00001	89
Omitting Akizawa et al. 2020	2782/2542	9	0.29	[0.12, 0.45]	3.43	0.0006	8	0.00001	84
Omitting Charytan et al. 2021	2526/2302	9	0.21	[-0.00, 0.42]	1.92	0.05	8	0.00001	90
Omitting Chen et al. 2017	2836/2651	9	0.18	[-0.01, 0.37]	1.87	0.06	8	0.00001	90
Omitting Chen et al. 2019	2692/2573	9	0.21	[0.01, 0.42]	2.07	0.04	8	0.00001	90
Omitting Hou et al. 2021	2810/2630	9	0.10	[-0.04, 0.24]	1.40	0.16	8	0.00001	79
Omitting NCT01888445. 2018	2833/2646	9	0.23	[0.03, 0.42]	2.27	0.02	8	0.00001	90
Omitting NCT02174731. 2020	1893/1657	9	0.24	[0.00, 0.47]	2.00	0.05	8	0.00001	89
Omitting NCT02278341. 2019	2483/2253	9	0.21	[-0.00, 0.43]	1.93	0.05	8	0.00001	90
Omitting Provenzano et al. 2016	2835/2651	9	0.23	[0.03, 0.42]	2.28	0.02	8	0.00001	90
Omitting Provenzano et al. 2021	2374/2152	9	0.22	[-0.00, 0.45]	1.95	0.05	8	0.00001	90

CI, confidence interval; df, degrees of freedom; SMD, standardized mean difference.