

Supplemental Content 2

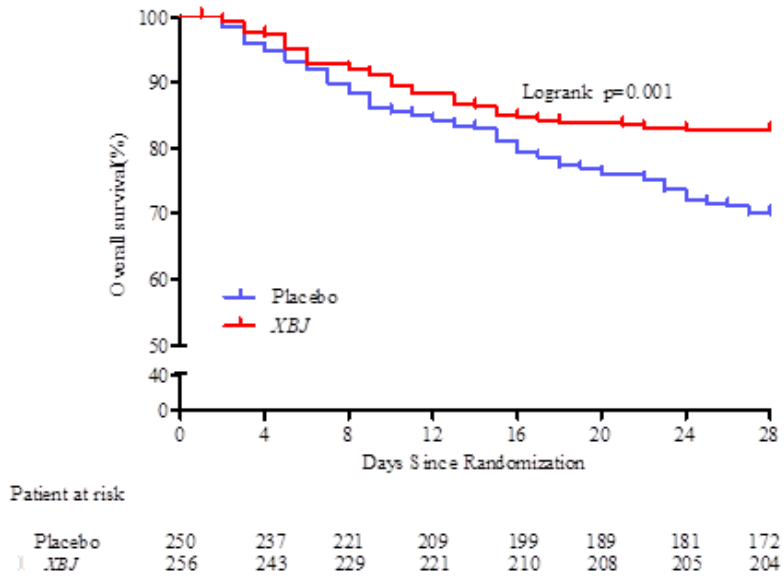


Figure S1. Kaplan-Meier analysis of the effect of XueBijing on 28-day survival (506 patients with pneumonia severity index class IV–V)

TABLE S1. Microbiologic identification for XueBiJing group vs placebo group using descriptive statistics for the intention-to-treat populations

		XueBiJing (n=334)	Placebo (n=341)	Total	<i>P value</i>
Microbiologic identification	Yes (%)	144(43.11%)	153(44.87%)	297(44.00%)	0.646
Etiology	Known (%)	85(59.03%)	104(67.97%)	189(63.64%)	0.109
Sensitivity tests	Known (%)	42(49.41%)	42(40.38%)	84(44.44%)	0.214

Table S2. Comparison of the secondary outcomes for the intention-to-treat populations

	XueBiJing (n=334)	Placebo (n=341)	Between-group different (95% CI)	P value
PSI score, mean(SD)				
Day 4	93.14(28.67)	100.01(29.24)	-8.73(-12.87,-4.59)	<0.0001
Day 8	87.91(29.90)	96.35(30.61)	-10.05(-14.67,-5.42)	<0.0001
PSI Improvement Rate				
Day 4	194/307(63.2%)	141/305(44.8%)	18.1% (10.5%-25.7%)	<0.0001
Sequential Organ Failure Assessment Score, mean(SD)				
Day 4	4.52(2.94)	5.01(2.89)	-0.58(-0.90,-0.25)	0.0005
Day 8	3.65(3.01)	4.44(2.95)	-0.78(-1.18,-0.39)	0.0001
Sequential Organ Failure Assessment high risk Rate				
Day 4	194/308 (62.99%)	218/315 (69.21%)	-6.2%(-13.2%, 0.8%)	0.098
Day 8	142/301 (47.18%)	192/306 (62.75%)	-15.6%(-23.7%,-7.5%)	0.0001
APACHE II score, mean (SD)				
Day 4	10.40(5.95)	12.00(6.09)	-1.59(-2.35,-0.83)	<0.0001
Day 8	9.19(6.46)	11.12(6.25)	-1.88(-2.79,-0.99)	<0.0001
APACHE II improvement Rate				
Day 4	22/308 (7.14%)	40/316 (12.66%)	-5.6% (-9.9%,-1.2%)	0.022
Day 8	23/301 (7.64%)	35/306 (11.44%)	-3.8% (-8.4%, 0.8%)	0.109
SIRS improvement Rate				
DAY 4	127/310 (40.97%)	91/315 (28.89%)	12.1% (4.3%-19.9%)	0.002
DAY 8	166/301 (55.15%)	142/305 (46.56%)	8.6% (1.0%-16.2%)	0.031
Lung Injury Score, mean(SD)				
Day 4	6.81(2.43)	7.30(2.64)	-0.43(-0.91,0.05)	0.083
Day 8	6.81(2.35)	7.49(2.88)	-0.34(-0.98,0.30)	0.295
Lung Injury Score improvement Rate				

Day 4	100/166 (60.24%)	87/175 (49.71%)	9.9% (1.0%-20.7%)	0.044
Day 8	97/151 (64.24%)	91/167 (54.49%)	10.5% (0.0%-21.3%)	0.049
MODS score, mean (SD)				
Day 4	5.35(3.41)	5.36(2.97)	-0.01(-0.89,0.88)	0.990
Day 8	4.18(3.81)	4.86(3.31)	0.69(-1.71,0.34)	0.189
MODS score improvement Rate				
Day 4	47/90(52.22%)	40/110(36.36%)	14.8% (0.7%-29.0%)	0.028
Day 8	62/80 (77.50%)	54/106 (50.94%)	26.3% (13.2%-39.4%)	0.0003
Body temperature, mean (SD)				
Day 4	37.39(0.78)	37.46(0.82)	-0.08(-0.19,0.04)	0.184
Day 8	37.18(0.69)	37.30(0.80)	-0.12(-0.23,0.00)	0.046
Oxygenation index, mean (SD)				
Day 4	246.82(98.86)	229.69(96.55)	17.34(2.16,32.52)	0.025
Day 8	269.90(105.76)	251.51(104.02)	15.54(-1.04,32.12)	0.066
Procalcitonin				
Day 4	5.54(19.49)	4.90(17.95)	1.97(-0.91,4.86)	0.180
Day 8	2.54(7.41)	4.69(26.42)	-1.85(-5.41,1.71)	0.309
C-reactive protein				
Day 4	59.91(67.23)	64.92(63.25)	-3.93(-13.01,5.14)	0.396
Day 8	38.53(51.46)	48.17(78.33)	-7.59(-18.43,3.24)	0.170
D-dimer				
Day 4	3475.39(5918.51)	2300.75(3355.61)	854.30(123.14,1585.45)	0.023
Day 8	2877.76(4355.08)	2416.28(4022.42)	259.13(-389.74,908.01)	0.434
Total duration of antibiotic use, days, mean(SD)	7.55(3.07)	7.65(3.09)	-0.09(-0.56,0.37)	0.678

TABLE S3. Adverse events and Clinically Significant Laboratory Abnormalities

Event		Placebo (n=341), n (%)		XueBiJing (n=334), n (%)	
Clinically Significant Laboratory Abnormalities	Low red blood cell count	16	16(4.69%)	22	22(6.59%)
	High red blood cell count	3	3(0.88%)	1	1(0.30%)
	Low hemoglobin count	27	27(7.92%)	22	22(6.59%)
	High hemoglobin count	2	2(0.59%)	1	1(0.30%)
	Low white blood cell count	4	4(1.17%)	3	3(0.90%)
	High white blood cell count	18	18(5.28%)	18	18(5.39%)
	Low platelet count	10	10(2.93%)	8	8(2.40%)
	High platelet count	9	9(2.64%)	6	6(1.80%)
	Low hematocrit levels	11	11(3.23%)	9	9(2.69%)
	High hematocrit levels	1	1(0.29%)	0	0(0.00%)
	Abnormal alanine aminotransferase	2	2(0.59%)	0	0(0.00%)
	Elevated alanine aminotransferase	31	31(9.09%)	30	30(8.98%)
	Decreased aspartate amino transferase	1	1(0.29%)	3	3(0.90%)
	Elevated aspartate amino transferase	18	18(5.28%)	22	22(6.59%)
	Decreased total bilirubin	1	1(0.29%)	2	2(0.60%)
	Elevated total bilirubin	12	12(3.52%)	9	9(2.69%)
	Decreased blood urea nitrogen	2	2(0.59%)	1	1(0.30%)
	Elevated blood urea nitrogen	20	20(5.87%)	20	20(5.99%)
	Decreased serum creatinine	8	8(2.35%)	5	5(1.50%)
	Elevated serum creatinine	11	11(3.23%)	9	9(2.69%)
	Elevated blood glucose	15	15(4.40%)	19	19(5.69%)
	Decreased K ⁺	11	11(3.23%)	7	7(2.10%)
	Elevated K ⁺	1	1(0.29%)	2	2(0.60%)
	Elevated Na ⁺	5	5(1.47%)	4	4(1.20%)

Event		Placebo (n=341), n (%)		XueBiJing (n=334), n (%)	
	Decreased Na ⁺	4	4(1.17%)	2	2(0.60%)
	Decreased plasma fibrinogen	3	3(0.88%)	2	2(0.60%)
	Elevated plasma fibrinogen	13	13(3.81%)	8	8(2.40%)
	Decreased prothrombin time	0	0(0.00%)	1	1(0.30%)
	Elevated prothrombin time	11	11(3.23%)	4	4(1.20%)
	Decreased activated partial thromboplastin time	1	1(0.29%)	0	0(0.00%)
	Elevated activated partial thromboplastin time	8	8(2.35%)	3	3(0.90%)
	Elevated fibrin D-dimer	6	6(1.76%)	5	5(1.50%)
	Elevated C reactive protein	1	1(0.29%)	0	0(0.00%)
	Elevated procalcitonin	1	1(0.29%)	0	0(0.00%)
	Positive protein in urine	1	1(0.29%)	3	3(0.90%)
	High urine white blood cell count	3	3(0.88%)	3	3(0.90%)
	High urine red blood cell count	3	3(0.88%)	3	3(0.90%)
	Elevated urine glucose	4	4(1.17%)	2	2(0.60%)
	Positive fecal occult blood test	1	1(0.29%)	0	0(0.00%)
	Total	299	135(39.59%)	259	117(35.03%)
Musculoskeletal and connective tissue diseases	Pain in the upper limbs	0	0(0.00%)	1	1(0.30%)
	Total	0	0(0.00%)	1	1(0.30%)
Immune system diseases	Allergic reactions	0	0(0.00%)	1	1(0.30%)
	Total	0	0(0.00%)	1	1(0.30%)
Skin and subcutaneous tissue diseases	Erythema	1	1(0.29%)	0	0(0.00%)
	Total	1	1(0.29%)	0	0(0.00%)
Systemic diseases and various responses at the site of administration	Shivering	1	1(0.29%)	0	0(0.00%)
	Total	1	1(0.29%)	0	0(0.00%)

Event		Placebo (n=341), n (%)		XueBiJing (n=334), n (%)	
Gastrointestinal system diseases	Upper digestive tract perforation	1	1(0.29%)	0	0(0.00%)
	Total	1	1(0.29%)	0	0(0.00%)
Blood and lymphatic system diseases	Anemia	2	2(0.59%)	0	0(0.00%)
	Total	2	2(0.59%)	0	0(0.00%)