Supplementary Tables

"Effects of carrimycin on biomarkers of inflammation and immune function in tumor patients with sepsis: A multicenter double-blind randomized placebo trial"

The trial was registered in the Chinese Clinical Trial Registry (http://www.chictr.org.cn) with the number ChiCTR2000032339.

This supplement contains the following items:

1. Baseline levels of primary and secondary outcome in the overall analysis and subgroups.
2. Analysis of adverse events.

Contents

Table S1 Baseline levels of primary outcome

Indicators	Placebo group	Carrimycin group	*P value*
HLA-DR (%), n	51	47	0.870
Median (*IQR*)	77.6 (66.2-95.1)	79.5 (65.5-92.1)	
HLA-DR group	51	47	0.464
＜30% (n, %)	4 (7.8)	2 (4.3)	
≥30-＜45% (n, %)	4 (7.8)	1 (2.1)	
≥35-＜85% (n, %)	22 (43.1)	26 (55.3)	
≥85% (n, %)	21 (41.2)	18 (38.3)	
IL-6 (pg/mL), n	52	47	0.385
Median (IQR)	66.7 (39.6-240.1)	129.8 (36.0-226.0)	
IL-8 (pg/mL), n	52	47	0.742
Median (*IQR*)	39.3 (20.9-120.9)	45.2 (22.7-88.2)	
IL-10 (pg/mL), n	52	47	0.377
Median (*IQR*)	2.4 (0.9-7.7)	2.3 (0.7-5.4)	
TNF-α (pg/mL), n	52	47	0.175
Median (*IQR*)	0.1 (0.0-0.7)	0.5 (0.0-0.8)	
PD-1 (pg/mL), n	52	47	0.804
Median *(IQR*)	40.7 (17.3-95.5)	43.4 (19.8-60.2)	
PD-1 in CD4+ (%), n	51	47	0.765
Median (*IQR*)	11.3 (4.2-22.5)	12.0 (6.3-20.0)	
PD-1 in CD8+ (%), n	51	47	0.562
Median (*IQR*)	10.2 (4.4-16.3)	10.5 (4.8-19.5)	
Monocytic-MDSC (%), n	51	47	0.550
Median *(IQR*)	2.2 (1.0-5.6)	2.4 (0.7-4.4)	
Granulocytic-MDSC (%), n	51	47	0.887
Median (*IQR*)	0.3 (0.1-0.8)	0.3 (0.2-0.8)	
CD4+ (%), n	51	47	0.771
Median (*IQR*)	38.7 (25.6-46.0)	36.1 (25.7-45.5)	
CD8+ (%), n	51	47	0.034
Median (*IQR*)	22.7 (12.2-27.9)	26.7 (18.6-33.1)	

IQR denotes interquartile range. mHLA-DR, monocyte hurman leukocyte antigen-DR; CD, cluster of differentiation.

Table S2 Baseline levels of secondary outcome

Indicators	Placebo group	Carrimycin group	*P value*
APHACHE II score, median (*IQR*)	14 (11-17)	14 (11-17)	0.952
SOFA score, median (*IQR*)			
Respiratory system	3 (2-3)	3 (2-3)	0.521
Coagulation	1 (0-2)	0 (0-1)	0.133
Liver	0 (0-1)	0 (0-1)	0.888
Cardiovascular system	0 (0-3.75)	3 (0-4)	0.188
Nervous system	0 (0-0)	0 (0-0)	0.442
Renal system	0 (0-0)	0 (0-0)	0.592
CRP (μg/mL), n	50	42	0.072
Median (*IQR*)	138.8 (94.3-220.4)	180.1 (123.4-239.5)	
PCT (ng/mL), n	51	45	0.582
Median (*IQR*)	3.3 (0.7-12.4)	3.6 (1.1-15.7)	

IQR denotes interquartile range. APHACHE II score denotes acute physiology and chronic health evaluation II, which ranges from 0 to 71, with higher scores indicating more severe disease. SOFA score denotes sequential organ failure assessment, which ranges from 0 to 24, with higher scores indicating more severe organ failure.

Table S3 Baseline levels of primary outcome in the CD4+<38.25 subgroup

Indicators	Placebo group （N=25）	Carrimycin group （N=25）	*P value*
HLA-DR (%), median (*IQR*)	68.9 (44.9-88.4)	78.6 (53.3-89.7)	0.432
HLA-DR group			0.585
＜30% (n, %)	2 (8)	2 (8)	
≥30-＜45% (n, %)	4 (16)	1 (4)	
≥35-＜85% (n, %)	11 (44)	13 (52)	
≥85% (n, %)	8 (32)	9 (36)	
IL-6 (pg/mL), median (*IQR*)	67.9 (19.8-235.7)	123.1 (40.3-268.3)	0.265
IL-8 (pg/mL), median (*IQR*)	62.8 (28.2-159.1)	48.4 (22.6-170.7)	0.621
IL-10 (pg/mL), median (*IQR*)	2.2 (1.2-7.9)	2.8 (1.2-9.0)	0.734
TNF-α (pg/mL), median (*IQR*)	0.2 (0.0-0.7)	0.5 (0.0-0.7)	0.434
PD-1 (pg/mL), median (*IQR*)	48.2 (17.3-97.9)	44.5 (20.5-63.4)	0.621
PD-1 in CD4+ (%), median (*IQR*)	19.1 (4.1-28.4)	12.7 (6.5-23.5)	0.946
PD-1 in CD8+ (%), median (*IQR*)	13.2 (2.9-19.4)	10.9 (4.6-19.8)	0.869
Monocytic-MDSC (%), median (*IQR*)	1.7 (0.7-4.0)	2.4 (0.7-4.8)	0.541
Granulocytic-MDSC (%), median (*IQR*)	0.3 (0.1-0.5)	0.4 (0.2-0.9)	0.19
CD4+ (%), median (*IQR*)	25.6 (19.1-34.4)	27.4 (21.6-32.3)	0.969
CD8+ (%), median (*IQR*)	20.7 (11.7-29.8)	26.7 (20.6-36.0)	0.077

IQR denotes interquartile range.

Table S4 Baseline levels of secondary outcome in the CD4+<38.25 subgroup

Indicators	Placebo group	Carrimycin group	*P value*
APHACHE II score, n	25	25	
Median (*IQR*)	15.0 (12.0-19.0)	15.0 (12.0-22.5)	0.534
SOFA score, n	25	25	
Respiratory system, median (*IQR*)	3.0 (1.5-3.0)	3.0 (2.0-3.0)	0.170
Coagulation, median (*IQR*)	1.0 (0.0-2.5)	0.0 (0.0-2.0)	0.161
Liver, median (*IQR*)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	1.000
Cardiovascular system, median (*IQR*)	1.0 (0.0-4.0)	3.0 (0.5-4.0)	0.316
Nervous system, median (*IQR*)	0.0 (0.0-0.0)	0.0 (0.0-2.0)	0.021
Renal system, median (*IQR*)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.406
CRP (μg/mL), n	23	22	
Median (*IQR*)	158.6 (99.6-233.7)	221.4 (103.5-252.7)	0.376
PCT (ng/mL), n	24	25	
Median (*IQR*)	4.0 (1.5-50.5)	7.2 (1.4-22.0)	0.749

IQR denotes interquartile range.

Table S5 Study clinical outcomes in the CD4+<38.25 subgroup

Secondary outcome	Placebo group（N=25）	Carrimycin group（N=25）	*P value*
Mortality at 28 days, n (%)	2(8)	0(0)	0.490
Mortality at 7 days, n (%)	1(4)	0(0)	1.000
Mechanical ventilation, n (%)	12(48)	16(64)	0.254
Duration of mechanical ventilation (d)			0.546
Median (*IQR*)	8.8(5.2-11.9)	7.0(4.3-11.5)	
ICU stay, n (%)	25(100)	24(96)	—
Duration of ICU (d)			0.779
Median (*IQR*)	9.7(8.0-13.4)	10.3(8.5-11.6)	
CRRT treatment, n (%)	4(16)	1(4)	0.349
Duration of CRRT treatment (d)			1.000
Median (*IQR*)	2.2(1.5-6.5)	1.7(1.7-1.7)	

IQR denotes interquartile range.

Table S6 Baseline levels of primary outcome in the CD8+<25.195 subgroup

Indicators	Placebo group （N=29）	Carrimycin group （N=20）	*P value*
HLA-DR (%), median (*IQR*)	83.9 (66.7-98.9)	85.0 (70.9-99.2)	0.722
HLA-DR group			0.317
＜30% (n, %)	4 (13.8)	0 (0.0)	
≥30-＜45% (n, %)	1 (3.4)	0 (0.0)	
≥35-＜85% (n, %)	11 (37.9)	10 (50.0)	
≥85% (n, %)	13 (44.8)	10 (50.0)	
IL-6 (pg/mL), median (*IQR*)	65.6 (38.4-296.9)	112.5 (40.7-225.2)	0.569
IL-8 (pg/mL), median (*IQR*)	47.8 (25.6-120.5)	43.6 (13.6-88.9)	0.246
IL-10 (pg/mL), median (*IQR*)	2.4 (1.0-7.9)	2.2 (0.7-4.3)	0.186
TNF-α (pg/mL), median (*IQR*)	0.0 (0.0-0.7)	0.1 (0.0-0.5)	0.965
PD-1 (pg/mL), median (*IQR*)	44.5 (13.2-96.3)	47.1 (14.0-62.1)	0.508
PD-1 in CD4+ (%), median (*IQR*)	9.1 (3.1-18.4)	8.1 (4.2-12.4)	0.737
PD-1 in CD8+ (%), median (*IQR*)	10.2 (3.7-16.1)	8.8 (3.6-17.2)	0.959
Monocytic-MDSC (%), median (*IQR*)	2.2 (1.0-6.0)	1.8 (0.4-4.8)	0.509
Granulocytic-MDSC (%), median (*IQR*)	0.5 (0.0-0.9)	0.2 (0.0-1.0)	0.967
CD4+ (%), median (*IQR*)	39.2 (24.9-48.2)	36.9 (21.3-49.5)	0.839
CD8+ (%), median (*IQR*)	13.2 (11.1-20.8)	18.1 (15.6-22.2)	0.057

IQR denotes interquartile range.

Table S7 Baseline levels of secondary outcome in the CD8+<25.195 subgroup

Indicators	Placebo group	Carrimycin group	*P value*
APHACHE II score, n	29	29	
Median (*IQR*)	14.0(10.0-16.5)	15.0(9.5-21.5)	0.354
SOFA score, n	29	29	
Respiratory system, median (IQR)	3.0(2.0-3.0)	3.0(2.0-3.0)	0.686
Coagulation, median (IQR)	1.0(0.0-2.0)	0.0(0.0-1.0)	0.169
Liver, median (IQR)	0.0(0.0-1.0)	0.0(0.0-1.0)	0.750
Cardiovascular system, median (IQR)	1.0(0.0-4.0)	3.0(0.0-4.0)	0.657
Nervous system, median (IQR)	0.0(0.0-0.0)	0.0(0.0-0.0)	0.316
Renal system, median (IQR)	0.0(0.0-0.5)	0.0(0.0-1.0)	0.580
CRP (μg/mL), n	28	17	
Median (*IQR*)	111.5 (66.8-220.0)	189.6 (129.3-230.4)	0.071
PCT (ng/mL), n	29	20	
Median (*IQR*)	3.7 (0.9-13.6)	5.8 (1.1-17.1)	0.662

IQR denotes interquartile range.

Table S8 Study clinical outcomes in the CD8+<25.195 subgroup

Secondary outcome	Placebo group （N=29）	Carrimycin group （N=20）	*P value*
Mortality at 28 days, n (%)	3(10.3)	2(10.0)	1.000
Mortality at 7 days, n (%)	0 (0.0)	0 (0.0)	—
Mechanical ventilation, n (%)	20(69.0)	11(55.0)	0.319
Duration of mechanical ventilation (d)			
Median (*IQR*)	5.1(1.9-10.0)	6.2(5.2-10.0)	0.536
ICU stay, n (%)	28(96.6)	20(100.0)	—
Duration of ICU (d)			
Median (*IQR*)	9.7(8.3-13.3)	8.4(6.3-10.4)	0.072
CRRT treatment, n (%)	4(13.8)	0(0.0)	0.135
Duration of CRRT treatment (d)			
Median (*IQR*)	1.6(0.7-11.4)	0.0(0.0-0.0)	—

IQR denotes interquartile range.

Table S9 Baseline levels of primary outcome in the APACHE II score⩾9 subgroup

Indicators	Placebo group （N=46）	Carrimycin group （N=42）	*P value*
HLA-DR (%), median (*IQR*)	83.9 (66.7-98.9)	85.0 (70.9-99.2)	0.799
HLA-DR group,n	45	42	0.392
＜30% (n, %)	4(8.7)	2(4.8)	
≥30-＜45% (n, %)	4(8.7)	1(2.4)	
≥35-＜85% (n, %)	19(41.3)	24(57.1)	
≥85% (n, %)	18(39.1)	15(35.7)	
IL-6 (pg/mL), median (*IQR*)	65.6 (38.4-296.9)	112.5 (40.7-225.2)	0.107
IL-8 (pg/mL), median (*IQR*)	47.8 (25.6-120.5)	43.6 (13.6-88.9)	0.96
IL-10 (pg/mL), median (*IQR*)	2.4 (1.0-7.9)	2.2 (0.7-4.3)	0.716
TNF-α (pg/mL), median (*IQR*)	0.0 (0.0-0.7)	0.1 (0.0-0.5)	0.188
PD-1 (pg/mL), median (*IQR*)	44.5 (13.2-96.3)	47.1 (14.0-62.1)	0.914
PD-1 in CD4+ (%), median (*IQR*)	9.1 (3.1-18.4)	8.1 (4.2-12.4)	0.757
PD-1 in CD8+ (%), median (*IQR*)	10.2 (3.7-16.1)	8.8 (3.6-17.2)	0.593
Monocytic-MDSC (%), median (*IQR*)	2.2 (1.0-6.0)	1.8 (0.4-4.8)	0.494
Granulocytic-MDSC (%), median (*IQR*)	0.5 (0.0-0.9)	0.2 (0.0-1.0)	0.936
CD4+ (%), median (*IQR*)	39.2 (24.9-48.2)	36.9 (21.3-49.5)	0.619
CD8+ (%), median (*IQR*)	13.2 (11.1-20.8)	18.1 (15.6-22.2)	0.056

IQR denotes interquartile range.

Table S10 Baseline levels of secondary outcome in the APACHEII scores⩾9 subgroup

Indicators	Placebo group	Carrimycin group	*P value*
APHACHE II score, n	46	42	
Median (*IQR*)	15.0(12.0-17.3)	15.0(11.8-17.5)	0.867
SOFA score, n	46	42	
Respiratory system, median (*IQR*)	3.0(2.0-3.0)	3.0(2.0-3.0)	0.583
Coagulation, median (*IQR*)	1.0(0.0-2.0)	0.0(0.0-2.0)	0.212
Liver, median (*IQR*)	0.0(0.0-1.0)	0.0(0.0-1.0)	0.969
Cardiovascular system, median (*IQR*)	0.0(0.0-3.3)	3.0(0.0-4.0)	0.069
Nervous system, median (*IQR*)	0.0(0.0-0.0)	0.0(0.0-0.0)	0.310
Renal system, median (*IQR*)	0.0(0.0-0.0)	0.0(0.0-1.0)	0.602
CRP (μg/mL), n	44	37	
Median (*IQR*)	134.6(95.6-221.2)	183.6(119.0-245.0)	0.079
PCT (ng/mL), n	45	40	
Median (*IQR*)	2.9(0.7-13.1)	7.0(1.3-17.5)	0.185

IQR denotes interquartile range.

Table S11 Study clinical outcomes in the APACHEII scores ⩾9 subgroup

Secondary outcome	Placebo group (N=46)	Carrimycin group(N=42)	*P value*
Mortality at 28 days, n (%)	4(8.7)	2(4.8)	0.678
Mortality at 7 days, n (%)	0(0.0)	0(0.0)	—
Mechanical ventilation, n (%)	28(60.9)	27(64.3)	0.741
Duration of mechanical ventilation (d)			
Median (*IQR*)	6.7(2.6-10.0)	5.5(4.1-9.7)	0.699
ICU stay, n (%)	45(97.8)	41(97.6)	—
Duration of ICU (d)			
Median (*IQR*)	9.3(7.4-12.4)	8.9(7.6-11.5)	0.799
CRRT treatment, n (%)	7(15.2)	1(2.4)	0.060
Duration of CRRT treatment (d)			
Median (*IQR*)	2.6(1.4-7.8)	1.7(1.7-1.7)	0.827

IQR denotes interquartile range.

Table S12 Adverse events by system organ class analysis

System organ classification (SOC)	Preferred term (PT)	Carrimycin group(n=47)		Placebo group(n=52)		Total(n=99)	
		Number of Times	Number of subjects(%)	Number of Times	Number of subjects(%)	Number of Times	Number of subjects(%)
Investigations		**151**	**46(97.9)**	**214**	**48(92.3)**	**365**	**94(94.9)**
	White blood cell count decreased	5	5(10.6)	3	3(5.8)	8	8(8.1)
	White blood cell count increased	35	29(61.7)	40	34(65.4)	75	63(63.6)
	Alanine aminotransferase increased	12	12(25.5)	20	18(34.6)	32	30(30.3)
	Red blood cell count decreased	6	6(12.8)	10	10(19.2)	16	16(16.2)
	Haematocrit decreased	6	6(12.8)	12	12(23.1)	18	18(18.2)
	White blood cells urine positive	2	2(4.3)	6	5(9.6)	8	7(7.1)
	Protein urine present	3	3(6.4)	6	5(9.6)	9	8(8.1)
	Red blood cells urine positive	3	2(4.3)	6	5(9.6)	9	7(7.1)
	Blood pressure systolic increased	1	1(2.1)	0	0(0.0)	1	1(1.0)

	Aspartate aminotransferase decreased	1	1(2.1)	0	0(0.0)	1	1(1.0)
	Aspartate aminotransferase increased	13	12(25.5)	25	22(42.3)	38	34(34.3)
	Electrocardiogram QT prolonged	2	2(4.3)	1	1(1.9)	3	3(3.0)
	Electrocardiogram T wave abnormal	1	1(2.1)	3	3(5.8)	4	4(4.0)
	Blood bilirubin increased	21	19(40.4)	19	19(36.5)	40	38(38.4)
	Haemoglobin decreased	3	3(6.4)	9	9(17.3)	12	12(12.1)
	Blood creatinine decreased	2	2(4.3)	6	5(9.6)	8	7(7.1)
	Blood creatinine increased	5	5(10.6)	5	5(9.6)	10	10(10.1)
	Blood urea decreased	1	1(2.1)	0	0(0.0)	1	1(1.0)
	Blood urea increased	6	6(12.8)	11	10(19.2)	17	16(16.2)
	Blood glucose increased	8	6(12.8)	8	8(15.4)	16	14(14.1)
	Platelet count decreased	10	10(21.3)	19	17(32.7)	29	27(27.3)
	Platelet count increased	2	2(4.3)	5	4(7.7)	7	6(6.1)
	Blood pressure increased	3	3(6.4)	0	0(0.0)	3	3(3.0)
Metabolism and nutrition disorders		**0**	**0(0.0)**	**2**	**2(3.8)**	**2**	**2(2.0)**
	Hyperglycaemia	0	0(0.0)	2	2(3.8)	2	2(2.0)
Injury, poisoning and procedural complications		**0**	**0(0.0)**	**1**	**1(1.9)**	**1**	**1(1.0)**

	Heart injury	0	0(0.0)	1	1(1.9)	1	1(1.0)
Respiratory, thoracic and mediastinal disorders		**0**	**0(0.0)**	**1**	**1(1.9)**	**1**	**1(1.0)**
	Pleural effusion	0	0(0.0)	1	1(1.9)	1	1(1.0)
General disorders and administration site conditions		**1**	**1(2.1)**	**0**	**0(0.0)**	**1**	**1(1.0)**
	Pyrexia	1	1(2.1)	0	0(0.0)	1	1(1.0)
Renal and urinary disorders		**13**	**12(25.5)**	**18**	**16(30.8)**	**31**	**28(28.3)**
	Proteinuria	13	12(25.5)	18	16(30.8)	31	28(28.3)
Gastrointestinal disorders		**15**	**5(10.6)**	**9**	**7(13.5)**	**24**	**12(12.1)**
	Nausea	1	1(2.1)	1	1(1.9)	2	2(2.0)
	Diarrhoea	9	4(8.5)	5	5(9.6)	14	9(9.1)
	Abdominal distension	0	0(0.0)	1	1(1.9)	1	1(1.0)
	Vomiting	5	3(6.4)	2	2(3.8)	7	5(5.1)
Cardiac disorders		**1**	**1(2.1)**	**1**	**1(1.9)**	**2**	**2(2.0)**
	Sinus tachycardia	1	1(2.1)	0	0(0.0)	1	1(1.0)
	Atrial fibrillation	0	0(0.0)	1	1(1.9)	1	1(1.0)
Vascular disorders		**3**	**2(4.3)**	**1**	**1(1.9)**	**4**	**3(3.0)**
	Hypotension	2	1(2.1)	0	0(0.0)	2	1(1.0)
	Hypertension	1	1(2.1)	0	0(0.0)	1	1(1.0)
	Hematuria	0	0(0.0)	1	1(1.9)	1	1(1.0)
Blood and lymphatic system disorders		**9**	**9(19.1)**	**10**	**9(17.3)**	**19**	**18(18.2)**
	Anaemia	9	9(19.1)	10	9(17.3)	19	18(18.2)

Table S13 Analysis of adverse events

	Carrimycin group(n=47)		Placebo group(n=52)		Total(n=99)		P Value
	Number of Times	Number of subjects(%)	Number of Times	Number of subjects(%)	Number of Times	Number of subjects(%)	
All adverse events	193	46(97.9)	257	49(94.2)	450	95(96.0)	0.683
Serious adverse events	0	0(0.0)	1	1(1.9)	1	1(1.0)	1.000
Adverse events led to drop-out[*1]	4	2(4.3)	4	2(3.8)	8	4(4.0)	1.000
Severity of all adverse events							
Mild	120	44(93.6)	175	48(92.3)	295	92(92.9)	0.296
Moderate	52	31(66.0)	51	26(50.0)	103	57(57.6)	
Severe	21	16(34.0)	31	20(38.5)	52	36(36.4)	
Outcome							
Disappeared without sequelae	93	38(80.9)	101	38(73.1)	194	76(76.8)	0.538
Disappeared with sequelae	1	1(2.1)	5	3(5.8)	6	4(4.0)	
continuing	50	28(59.6)	79	31(59.6)	129	59(59.6)	
Recovering	10	7(14.9)	10	6(11.5)	20	13(13.1)	
Aggravated	4	3(6.4)	15	9(17.3)	19	12(12.1)	
Death	0	0(0.0)	0	0(0.0)	0	0(0.0)	
Lost to follow up	35	17(36.2)	47	14(26.9)	82	31(31.3)	

Relationship to investigational products							
Definitely related	0	0(0.0)	0	0(0.0)	0	0(0.0)	0.780
Probably related	16	5(10.6)	10	7(13.5)	26	12(12.1)	
Possible related	40	23(48.9)	62	29(55.8)	102	52(52.5)	
Unlikely related	105	38(80.9)	152	44(84.6)	257	82(82.8)	
Not Related	32	16(34.0)	33	13(25.0)	65	29(29.3)	
Adverse reactions[*2]	56	26(55.3)	72	34(65.4)	128	60(60.6)	0.306
Serious adverse reactions	0	0(0.0)	1	1(1.9)	1	1(1.0)	1.000
Severity of all adverse reactions							
Mild	35	20(42.6)	50	27(51.9)	85	47(47.5)	0.521
Moderate	15	11(23.4)	13	13(25.0)	28	24(24.2)	
Severe	6	6(12.8)	9	6(11.5)	15	12(12.1)	

[*1]: The main reason for the subject to withdraw early is to select the adverse events involved in "adverse events".

[*2]: Definitely related, probably related, possibly related are classified as adverse reactions.