

TABLE S1: Antibiotic treatment-induced changes in total body weights in *M. tuberculosis*-infected guinea pigs

Month	Untreated	RHZ	PaMZ	PaM	Paz	MZ	PA	M	Z
-1.5	319.25 ± 19.04								
0	512.33 ± 41.95								
0.5	610.08 ± 58.09	428.75 ± 73.34	448.4 ± 39.66	469.35 ± 41.15	528.93 ± 58.52	509.05 ± 38.62	537.18 ± 12.62	536.08 ± 51.83	591.25 ± 79.92
1	674.43 ± 98.64	457.82 ± 63.56	486.67 ± 25.67	503.5 ± 10.77	534.4 ± 29.43	549 ± 26.15	592.93 ± 62.06	600.5 ± 37.47	601.08 ± 37.24
2	613.7 ± 89	484.5 ± 31.52	525.5 ± 11.61*						
1(+3)		757.49 ± 79.9	750.9 ± 86.1						
2(+3)		706.6 ± 38.4	718.9 ± 50.3						

Weights (arithmetic means and standard deviations in grams) of 4 guinea pigs for Month 0 to Month 2 and 10 guinea pigs for relapse time point are shown.

*Differences between the RHZ and PaMZ groups was statistically significant ($P = 0.05$).

R, rifampin; H, isoniazid; Z, pyrazinamide; Pa, Pa824; M, moxifloxacin.

(+3) indicates that guinea pigs was held for 3 months after treatment completion before sacrifice for relapse assessment.

TABLE S2: Antibiotic treatment reduces lung and spleen weights in *M. tuberculosis*-infected guinea pigs

Organ	Month	Untreated	RHZ	PaMZ	PaM	Paz	MZ	PA	M	Z
Lung [†]	- 1.5	2.44±0.4								
	0	2.24±0.16								
	0.5	2.53±0.52	1.83±0.28	1.91±0.19	2.1±0.32	2.43±0.43	2.1±0.26	2.12±0.38	1.97±0.16	2.8±0.6
	1	2.92±0.34	1.71±0.26	1.65±0.15	1.95±0.16	2.75±0.62	2.34±0.85	1.95±0.2	2.11±0.29	2.31±0.35
	2	2.97±0.5	1.89 ±0.37	1.74 ±0.04						
	1(+3)		1.78±0.3	1.78±0.2						
	2(+3)		1.76±0.2	1.77±0.2						
Spleen ^{††}	- 1.5	0.57±0.08								
	0	0.95±0.37								
	0.5	1.16±0.68	0.54±0.32	0.64 ± 0.15	0.83±0.51	1.33±0.31	0.63±0.12	0.92±0.2	0.78±0.56	1.92±0.93
	1	2.43±2.78	0.44±0.09	0.42 ± 0.05	0.53±0.15	0.82±0.12	0.51±0.11	0.56±0.12	0.59±0.09	0.73±0.31
	2	1.75±0.7	0.47±0.05	0.43 ± 0.06						
	1(+3)		0.41±0.2	0.55 ± 0.1						
	2(+3)		0.60.1±	0.59 ± 0.2						

*Normalized weights (arithmetic means and standard deviations in grams) of 4 guinea pigs per time point are shown.

[†]Differences between the RHZ and PaMZ groups were not statistically significant (P = 0.66, 0.72 and 0.48 at Month 0.5, Month1 and Month 2, respectively).

^{††}Differences between the RHZ and PaMZ groups were not statistically significant (P = 0.61, 0.66 and 0.36 at Month 0.5, Month1 and Month 2, respectively).

R, rifampin; H, isoniazid; Z, pyrazinamide; Pa, Pa824; M, moxifloxacin.

(+3) indicates that guinea pigs was held for 3 months after treatment completion before sacrifice for relapse assessment.

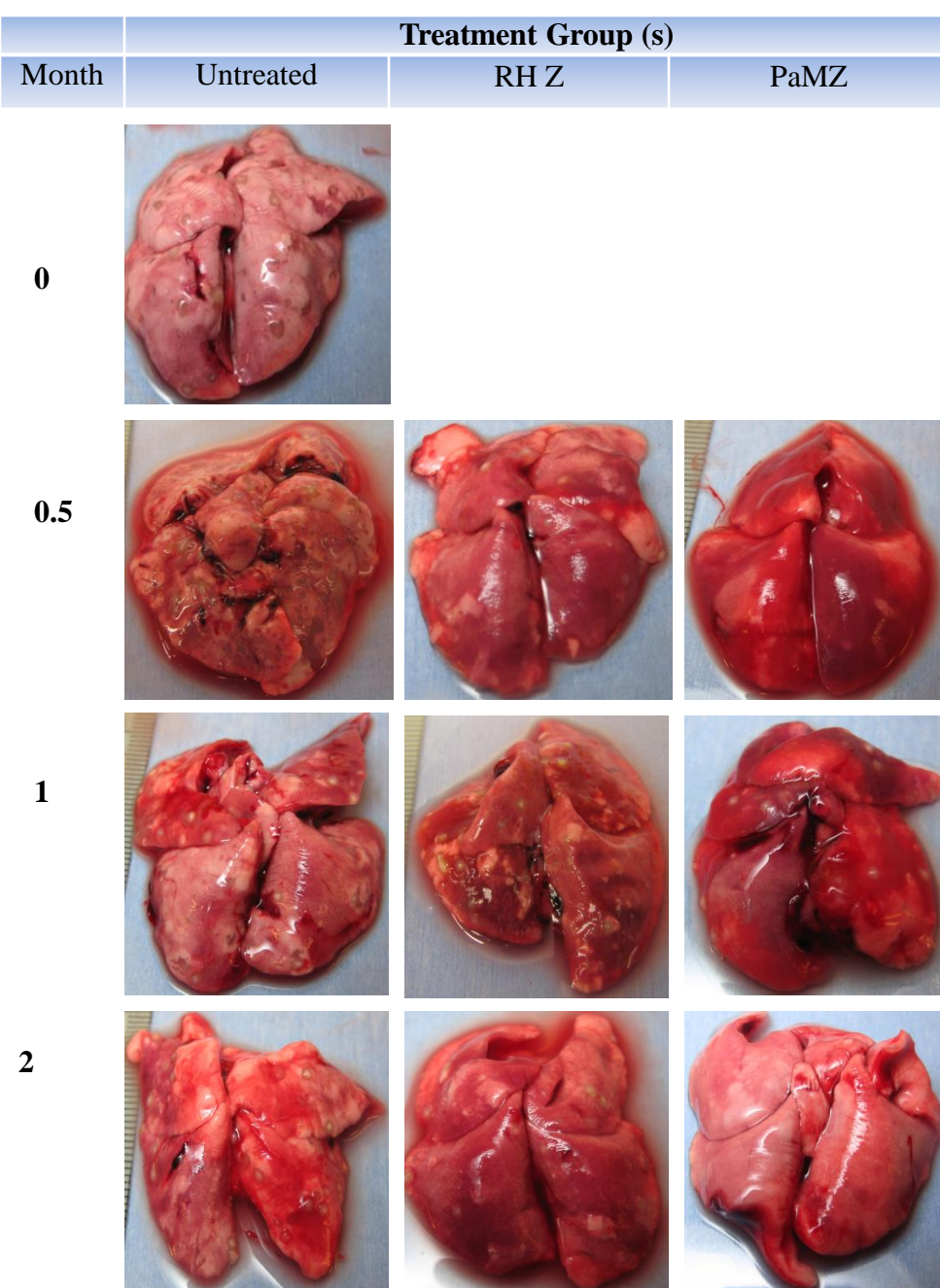


FIGURE S1: Gross pathology of infected guinea pig lungs during treatment. Images represent median lung weight samples of each indicated group.

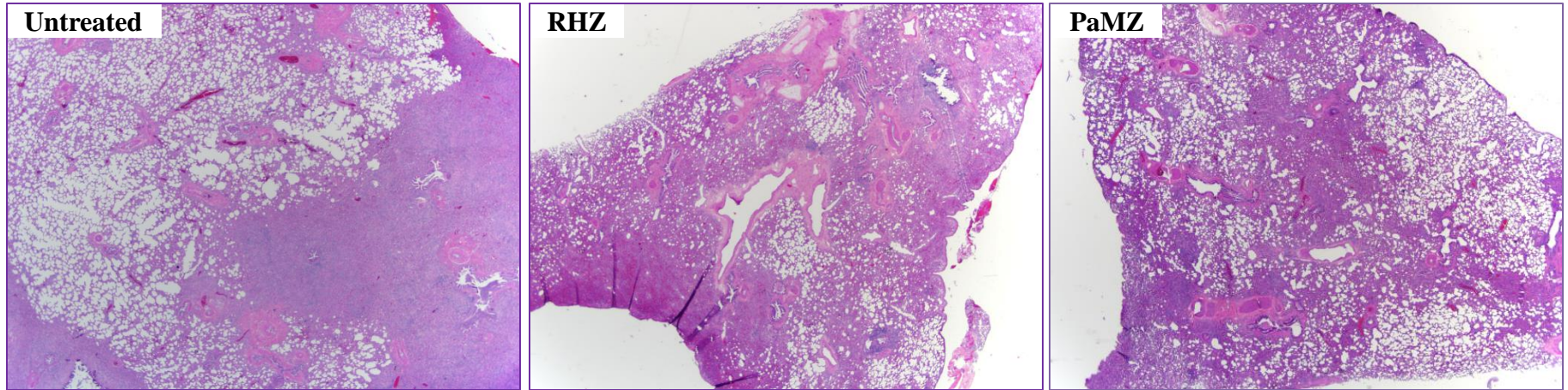


FIGURE S2: The combination regimens RHZ and PaMZ significantly reduce lung lesion size and number in *M. tuberculosis*-infected guinea pigs at Month 1 after treatment.

The untreated samples show diffuse inflammation and nodular aggregates and multiple small non-necrotizing granulomas. Both RHZ and PaMZ show diffuse inflammation with nodular aggregates and extension of the inflammation into airspaces. The multiple non-necrotizing granulomas seen in the untreated group are not seen in the RHZ- and PaMZ-treated groups.

Photomicrographs are representative sections of lungs from individual animals that best represents the mean values of 4 animals. Magnification =20 X.

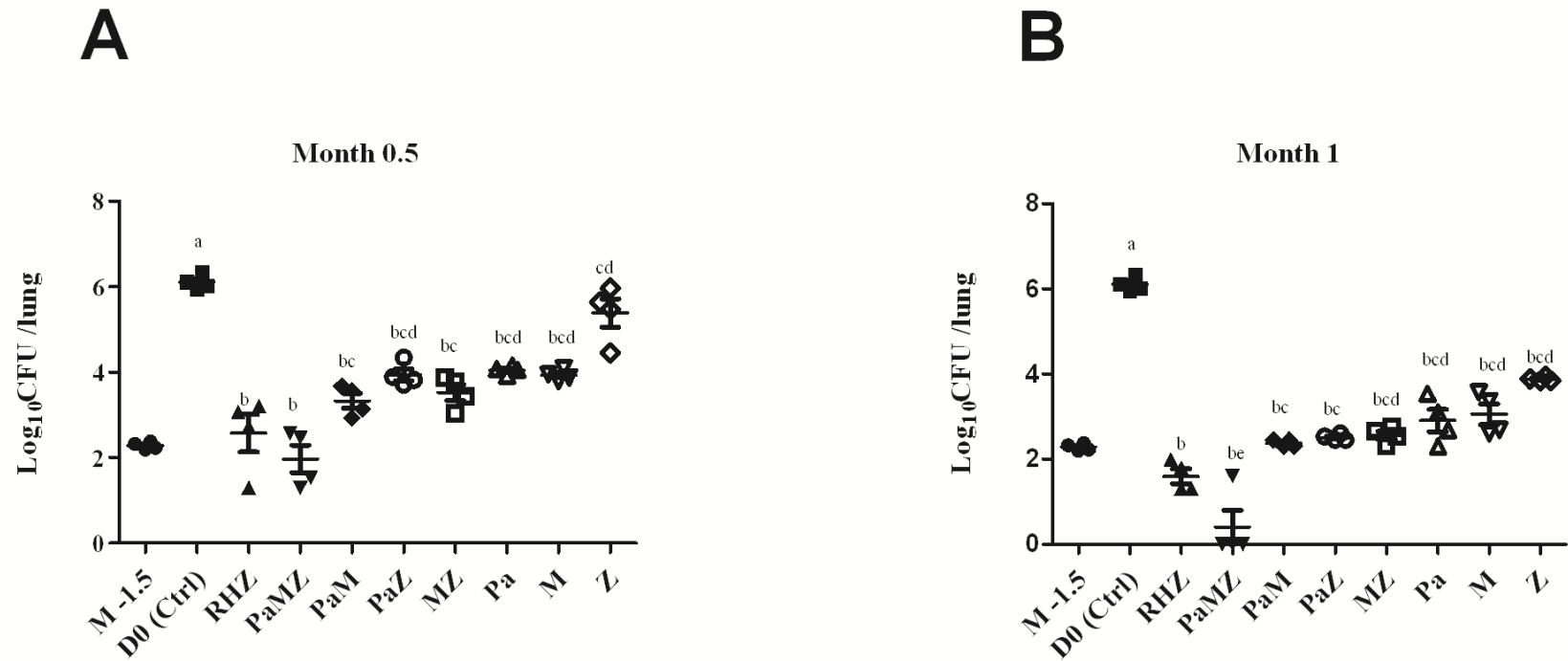


FIGURE S3: Mean (\pm SD) *Mycobacterium tuberculosis* lung colony-forming unit counts (CFU) after 2 weeks (Month 0.5, A) and 4 weeks (Month 1, B) of treatment.

Animals were infected via aerosol with $\sim 10^2$ colony-forming units (CFU) of *M. tuberculosis* H37Rv and were either left untreated (Day 0 control) or treated with drugs beginning on Month 1.5 after infection.

Abbreviations: Pa, Pa-824; M, moxifloxacin; R, rifampin; H, isoniazid; Z, pyrazinamide.

Significant differences were noted ($p < 0.05$) between (a) Month -1.5 (M -1.5) and Day 0 (D0) untreated control; (b) Day 0 untreated control and each treatment group; (c) PaMZ and single and two-drug treatment groups; (d) RHZ and single and two-drug treatment groups; (e) RHZ and PaMZ ($p < 0.001$).