

Synergistic Activity between Statins and Bisphosphonates against Acute Experimental Toxoplasmosis

Zhu-Hong Li^a, Catherine Li^a, Sergio H. Szajnman^b, Juan B. Rodriguez^b and Silvia N. J. Moreno^{*a}

Supplemental Material

Table S1: Cytotoxicity tests against fibroblasts

C7S (X IC₅₀)	% Inhibition
7 X	0.07 ± 2.69
4 X	0.73 ± 3.26
1 X	0.32 ± 1.01
0.5 X	0.39 ± 4.11

Atorvastatin (X IC₅₀)	% Inhibition
7 X	40.43 ± 1.79
4 X	14.07 ± 0.82
1 X	8.27 ± 0.06
0.5 X	10.01 ± 1.54

Combinations (IC₅₀ of each drug)	%Inhibition
7 X	48.23 ± 0.63
5 X	18.18 ± 2.93
4 X	12.68 ± 1.30
2 X	6.42 ± 1.94
1 X	10.72 ± 2.00
0.5 X	12.74 ± 1.09

Results are expressed as means ± SD of three independent experiments.

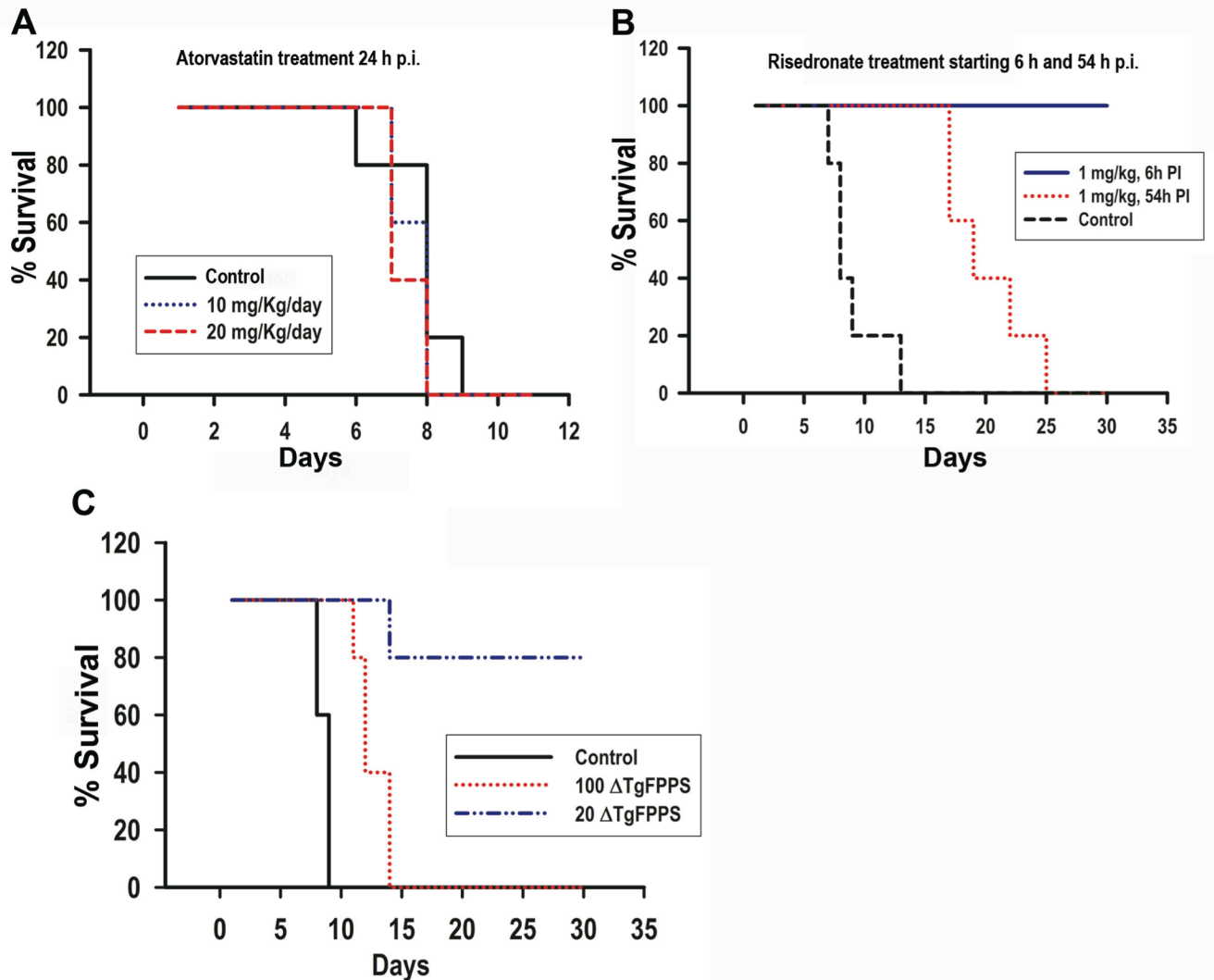


FIG. S1. Effects of starting time and number of tachyzoites of RH and *DTgfpps* strains on mice survival. (A) Atorvastatin treatment (10 and 20 mg/Kg/day) starting 24 h after infection with 20 RH tachyzoites. Statistical analysis using the Kaplan-Meier long rank test indicated there are no significant differences ($P > 0.05$) between the control and treated animals. (B) Risedronate treatment (1 mg/Kg/day) starting 6 or 54 h after the initial infection. (C) Infection with 20 and 100 parasites of a strain of lower virulence (*DTgfpps*). Atorvastatin treatment (20 mg/kg/day) starting 6 h p.i. In all cases treatment was once a day for 10 days. Statistical analysis using the Kaplan-Meier long rank test indicated that the survival curves (B and C) are significantly different ($P < 0.001$).

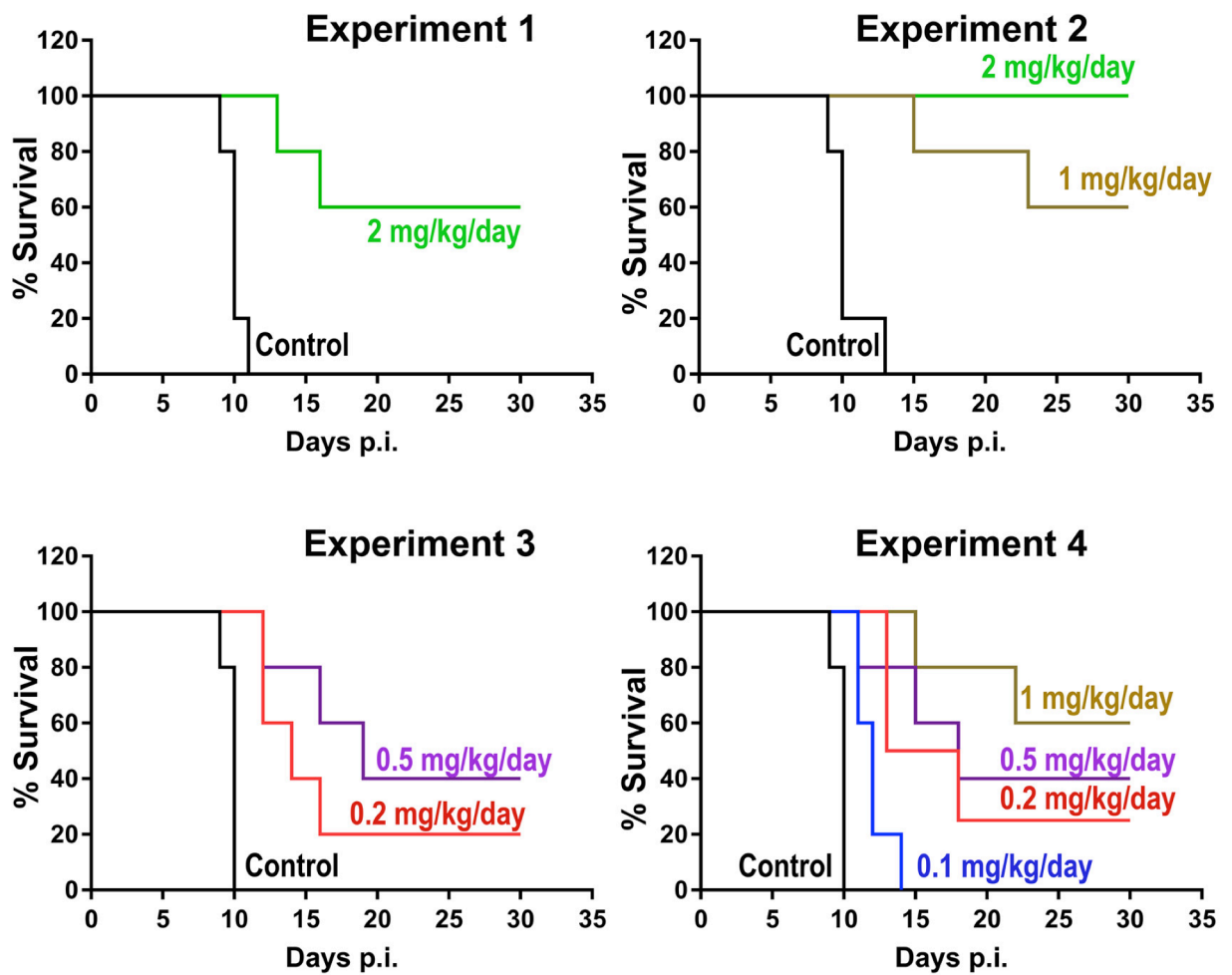


FIG. S2. Individual in vivo experiments testing different doses of C7S. Five mice were used for each group. Treatment started 6 hours after the initial infection with tachyzoites and continued daily for 10 days. Control mice received only the solvent used for the drugs. Other experimental details are under Materials and Methods.

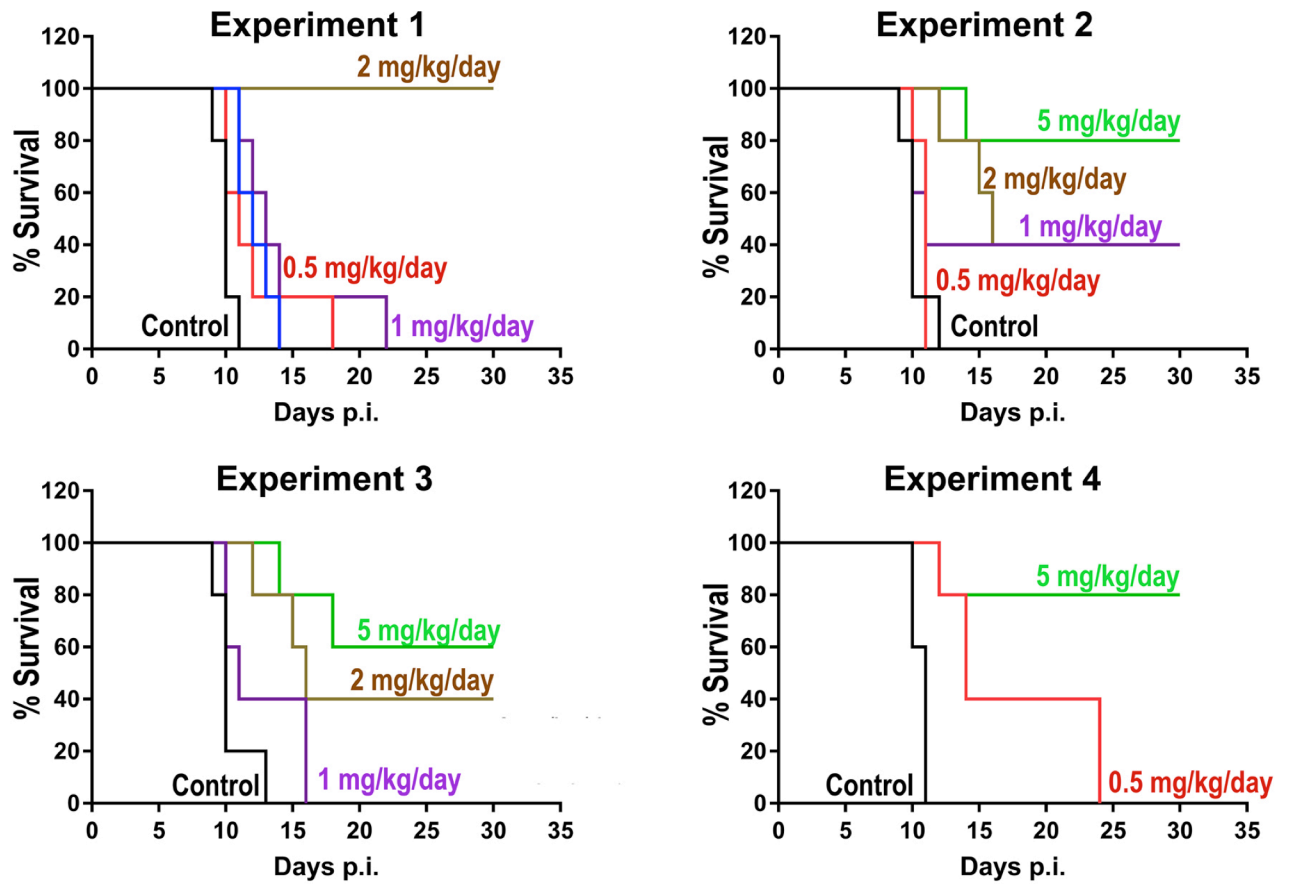


FIG. S3. Individual *in vivo* experiments testing different doses of atovaquone. Five mice were used for each group. Treatment started 6 hours after the initial infection with tachyzoites and was done daily for 10 days. Control mice received only the solvent used for the drugs. Other experimental details are under Materials and Methods.