Table S1. Experimental Scheme. The number of footpads (i.e., 2 per mouse) planned to be assessed for CFU analysis at each time point are shown.
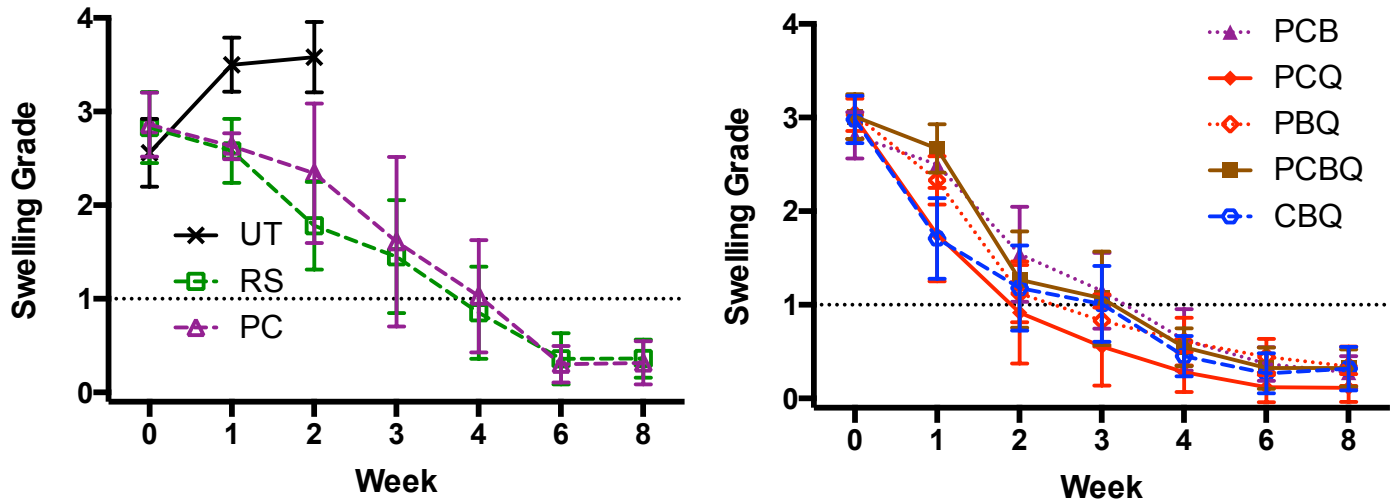
	D-46	D0	W1	W2	W4	W2+12	W4+21	W6+20	Total
Untreated	6	6	6	6	6				15
$RIF_{10}+STR_{150}$			6	6	6	20	20	20	29
$RPT_{20}+CFZ_{12.5}$			6	6	6	20	20		29
Tests									
$RPT_{20}+CFZ_{12.5}+BDQ_{25}$			6	6	6	20	20		29
$RPT_{20}+CFZ_{12.5}+Q203_{10}$			6	6	6	20	20		29
$RPT_{20}+BDQ_{25}+Q203_{10}$			6	6	6	20	20		29
$RPT_{20}+CFZ_{12.5}+BDQ_{25}+Q203_{10}$			6	6	6	20	20		29
$CFZ_{12.5}+BDQ_{25}+Q203_{10}$			6	6	6	20	20		29
Total	**6**	**6**	**24**	**24**	**24**	**70**	**70**	**20**	**228**

Table S2. Mouse footpad swelling grades (mean±s.d.) at Day 0 and during treatment

	Treatment Groups*							
Week	**UT**	**RS**	**PC**	**PCB**	**PCQ**	**PBQ**	**PCBQ**	**CBQ**
0	2.56±0.36	2.83±0.38	2.86±0.34	2.81±0.25	3.00±0.23	3.03±0.17	3.01±0.24	2.98±0.25
1	3.50±0.289	2.58±0.34	2.63±0.14	2.50±0.00	1.75±0.50	2.33±0.26	2.67±0.26	1.71±0.43
2	3.58±0.38	1.78±0.47	2.34±0.75	1.54±0.51	0.92±0.54	1.12±0.31	1.27±0.51	1.18±0.46
3		1.45±0.60	1.61±0.90	1.15±0.41	0.55±0.42	0.83±0.28	1.07±0.50	1.01±0.41
4		0.85±0.49	1.03±0.60	0.63±0.33	0.28±0.21	0.61±0.26	0.55±0.20	0.45±0.21
6		0.358±0.27	0.30±0.19	0.37±0.18	0.12±0.16	0.44±0.19	0.33±0.22	0.27±0.21
8		0.363±0.20	0.32±0.23	0.28±0.17	0.11±0.15	0.34±0.21	0.33±0.20	0.32±0.23

*UT= Untreated; RS= $RIF_{10}+STR_{150}$; PC= $RPT_{20}+CFZ_{12.5}$;

PCB= $RPT_{20}+CFZ_{12.5}+BDQ_{25}$; PCQ= $RPT_{20}+CFZ_{12.5}+Q203_{10}$;PBQ= $RPT_{20}+BDQ_{25}+Q203_{10}$;

PCBQ= $RPT_{20}+CFZ_{12.5}+BDQ_{25}+Q203_{10}$; CBQ= $CFZ_{12.5}+BDQ_{25}+Q203_{10}$

Fig. S1. Mean (± sd) footpad swelling grades by treatment group and treatment duration

Tables S3. Results of statistical analyses
Tables S3a-h: Test the efficacy of each Test Regimen compared to the RS control in terms of
footpad swelling (S3a-f) and CFU reduction (S3g-h) at the indicated time points.

S3a. Week 1 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
RS vs. PCB	0.08333	No	> 0.9999
RS vs. PCQ	0.8333	Yes	0.0009
RS vs. PBQ	0.2500	No	> 0.9999
RS vs. PCBQ	-0.08333	No	> 0.9999
RS vs. CBQ	0.8750	Yes	0.0005

S3b. Week 2 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
RS vs. PCB	0.2393	Yes	0.0283
RS vs. PCQ	0.8595	Yes	< 0.0001
RS vs. PBQ	0.6624	Yes	< 0.0001
RS vs. PCBQ	0.5085	Yes	< 0.0001
RS vs. CBQ	0.5999	Yes	< 0.0001

S3c. Week 3 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
RS vs. PCB	0.2986	Yes	0.0040
RS vs. PCQ	0.8964	Yes	< 0.0001
RS vs. PBQ	0.6192	Yes	< 0.0001
RS vs. PCBQ	0.3801	Yes	0.0001
RS vs. CBQ	0.4399	Yes	< 0.0001

S3d. Week 4 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value

RS vs. PCB	0.2273	Yes	0.0012
RS vs. PCQ	0.5697	Yes	< 0.0001
RS vs. PBQ	0.2447	Yes	0.0004
RS vs. PCBQ	0.3034	Yes	< 0.0001
RS vs. CBQ	0.4012	Yes	< 0.0001

S3e. Week 6 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
RS vs. PCB	-0.01042	No	> 0.9999
RS vs. PCQ	0.2396	Yes	< 0.0001
RS vs. PBQ	-0.08542	No	0.2667
RS vs. PCBQ	0.03333	No	> 0.9999
RS vs. CBQ	0.08958	No	0.2140

S3f. Week 8 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
RS vs. PCB	0.08375	No	0.1894
RS vs. PCQ	0.2500	Yes	< 0.0001
RS vs. PBQ	0.01875	No	> 0.9999
RS vs. PCBQ	0.0375	No	> 0.9999
RS vs. CBQ	0.04375	No	> 0.9999

S3g. Week 1 CFU

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
RS vs. PCB	0.3967	No	> 0.9999
RS vs. PCQ	1.063	No	0.0513
RS vs. PBQ	1.473	Yes	0.0033
RS vs. PCBQ	1.065	No	0.0507
RS vs. CBQ	2.027	Yes	< 0.0001

S3h. Week 2 CFU

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
RS vs. PCB	2.658	Yes	0.0006
RS vs. PCQ	4.382	Yes	< 0.0001
RS vs. PBQ	3.297	Yes	< 0.0001
RS vs. PCBQ	4.482	Yes	< 0.0001
RS vs. CBQ	3.112	Yes	< 0.0001

Tables S3i-p: Test the efficacy of each Test Regimen compared to the PC control in terms of footpad swelling (S3i-n) and CFU reduction (S3o-p) at the indicated time points.

S3i. Week 1 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PC vs. PCB	0.1250	No	> 0.9999
PC vs. PCQ	0.8750	Yes	0.0002
PC vs. PBQ	0.2917	No	0.5845
PC vs. PCBQ	-0.04167	No	> 0.9999
PC vs. CBQ	0.9167	Yes	< 0.0001

S3j. Week 2 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PC vs. PCB	0.8015	Yes	< 0.0001
PC vs. PCQ	1.422	Yes	< 0.0001
PC vs. PBQ	1.225	Yes	< 0.0001
PC vs. PCBQ	1.071	Yes	< 0.0001
PC vs. CBQ	1.162	Yes	< 0.0001

S3k. Week 3 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PC vs. PCB	0.4558	Yes	0.0002
PC vs. PCQ	1.054	Yes	< 0.0001
PC vs. PBQ	0.7764	Yes	< 0.0001
PC vs. PCBQ	0.5373	Yes	< 0.0001
PC vs. CBQ	0.5971	Yes	< 0.0001

S3l. Week 4 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PC vs. PCB	0.4034	Yes	< 0.0001
PC vs. PCQ	0.7458	Yes	< 0.0001
PC vs. PBQ	0.4208	Yes	< 0.0001
PC vs. PCBQ	0.4795	Yes	< 0.0001
PC vs. CBQ	0.5773	Yes	< 0.0001

S3m. Week 6 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PC vs. PCB	-0.06612	No	0.6740
PC vs. PCQ	0.1839	Yes	0.0002
PC vs. PBQ	-0.1411	Yes	0.0078
PC vs. PCBQ	-0.02237	No	> 0.9999
PC vs. CBQ	0.03388	No	> 0.9999

S3n. Week 8 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PC vs. PCB	0.03704	No	> 0.9999
PC vs. PCQ	0.2033	Yes	< 0.0001
PC vs. PBQ	-0.02796	No	> 0.9999
PC vs. PCBQ	-0.009211	No	> 0.9999
PC vs. CBQ	-0.002961	No	> 0.9999

S3o. Week 1 CFU

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PC vs. PCB	0.4750	No	> 0.9999
PC vs. PCQ	1.142	Yes	0.0296
PC vs. PBQ	1.552	Yes	0.0018
PC vs. PCBQ	1.143	Yes	0.0293
PC vs. CBQ	2.105	Yes	< 0.0001

S3p. Week 2 CFU

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PC vs. PCB	1.579	No	0.1502
PC vs. PCQ	3.303	Yes	0.0003
PC vs. PBQ	2.218	Yes	0.0166
PC vs. PCBQ	3.403	Yes	0.0002
PC vs. CBQ	2.033	Yes	0.0324

Tables S3q-x: Test if each drug in the 4-drug regimen (PCBQ) can be removed singly (i.e., yielding a 3-drug regimen) without loss of efficacy in terms of footpad swelling (S3q-v) and CFU reduction (S3w-x) at the indicated time points.

S3q. Week 1 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PCBQ vs. PCB	0.1667	No	> 0.9999
PCBQ vs. PCQ	0.9167	Yes	0.0003
PCBQ vs. PBQ	0.3333	No	0.3972
PCBQ vs. CBQ	0.9583	Yes	0.0002

S3r. Week 2 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PCBQ vs. PCB	-0.2692	Yes	0.0162
PCBQ vs. PCQ	0.3510	Yes	0.0008
PCBQ vs. PBQ	0.1538	No	0.3943
PCBQ vs. CBQ	0.09135	No	> 0.9999

S3s. Week 3 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PCBQ vs. PCB	-0.08152	No	> 0.9999
PCBQ vs. PCQ	0.5163	Yes	< 0.0001
PCBQ vs. PBQ	0.2391	Yes	0.0213
PCBQ vs. CBQ	0.05978	No	> 0.9999

S3t. Week 4 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PCBQ vs. PCB	-0.07609	No	0.5664
PCBQ vs. PCQ	0.2663	Yes	< 0.0001
PCBQ vs. PBQ	-0.05870	No	> 0.9999
PCBQ vs. CBQ	0.09783	No	0.2367

S3u. Week 6 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PCBQ vs. PCB	-0.04375	No	> 0.9999
PCBQ vs. PCQ	0.2063	Yes	< 0.0001
PCBQ vs. PBQ	-0.1188	Yes	0.0277
PCBQ vs. CBQ	0.05625	No	0.7902

S3v. Week 8 Swelling

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PCBQ vs. PCB	0.04625	No	> 0.9999
PCBQ vs. PCQ	0.2125	Yes	< 0.0001
PCBQ vs. PBQ	-0.01875	No	> 0.9999
PCBQ vs. CBQ	0.00625	No	> 0.9999

S3w. Week 1 CFU

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PCBQ vs. PCB	-0.6683	No	0.4859
PCBQ vs. PCQ	-0.001667	No	> 0.9999
PCBQ vs. PBQ	0.4083	No	> 0.9999
PCBQ vs. CBQ	0.9617	No	0.1186

S3x. Week 2 CFU

Bonferroni's multiple comparisons test	Mean Diff.	Significant?	Adjusted P Value
PCBQ vs. PCB	-1.823	Yes	0.0393
PCBQ vs. PCQ	-0.1000	No	> 0.9999
PCBQ vs. PBQ	-1.185	No	0.3253
PCBQ vs. CBQ	-1.370	No	0.1839