

A drug discovery journey

Combination of N⁶-methyltubercidin and miltefosine is curative in a *Leishmania amazonensis* mouse model

LBC website



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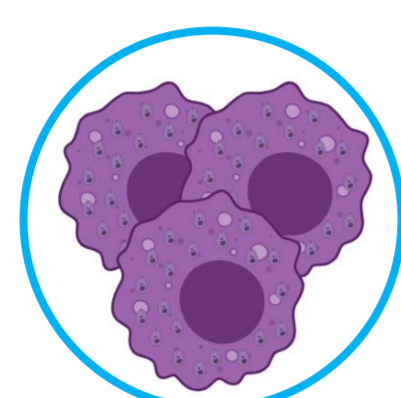
LMPH website



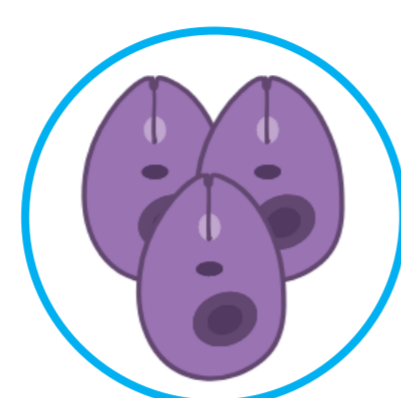
Introduction and aims

Explore the antileishmanial activity of N⁶-methyltubercidin (CL5564) against *L. amazonensis*, compared to the reference drug miltefosine (ML)

IN VITRO

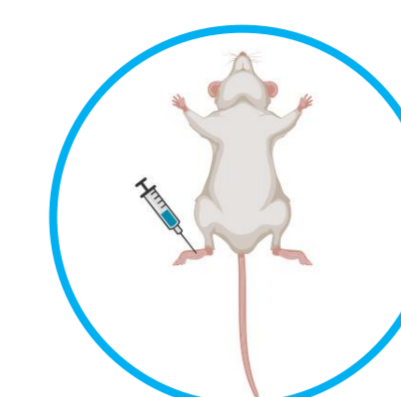


On intracellular amastigotes in macrophages



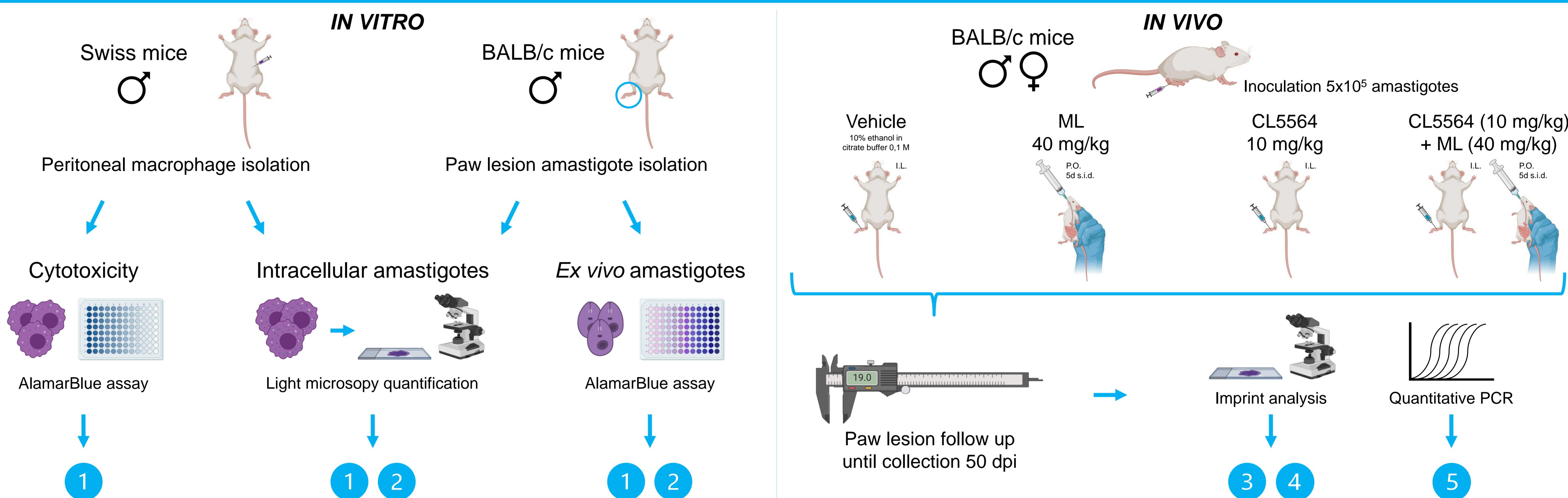
On ex vivo amastigotes (in combination with ML)

IN VIVO



On infected mice via intraslesional treatment (in combination with ML)

Experimental design



Key message and major findings

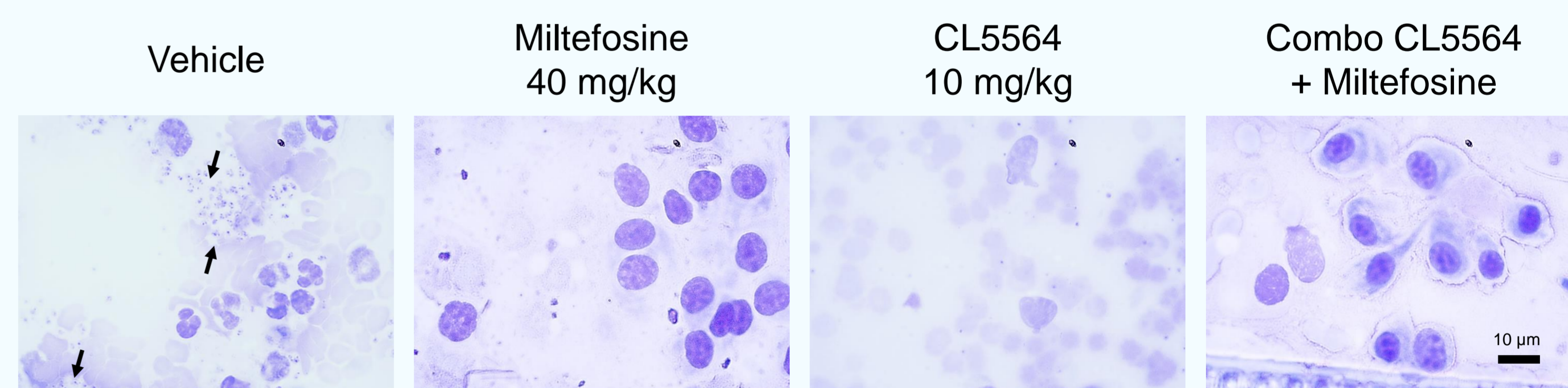
The nucleoside analogue N⁶-methyltubercidin (CL5564) is an appropriate alternative antileishmanial drug treatment

1 CL5564 is 6.5-fold more potent than ML

	IC ₅₀ (µM)		IC ₉₀ (µM)	Toxicity	
	Ex vivo	Intracellular	Intracellular	CC ₅₀ (µM)	SI
Miltefosine	1.54 ± 0.86	3.20 ± 0.66	10.49 ± 3.87	138.87 ± 15.70	43
CL5564	0.41 ± 0.41 ^a	0.56 ± 0 ^b	1.01 ± 0 ^c	155.40 ± 75.39 ^d	278

^ap = 0.03, ^bp = 0.0002, ^cp = 0.003, ^dp = 0.002

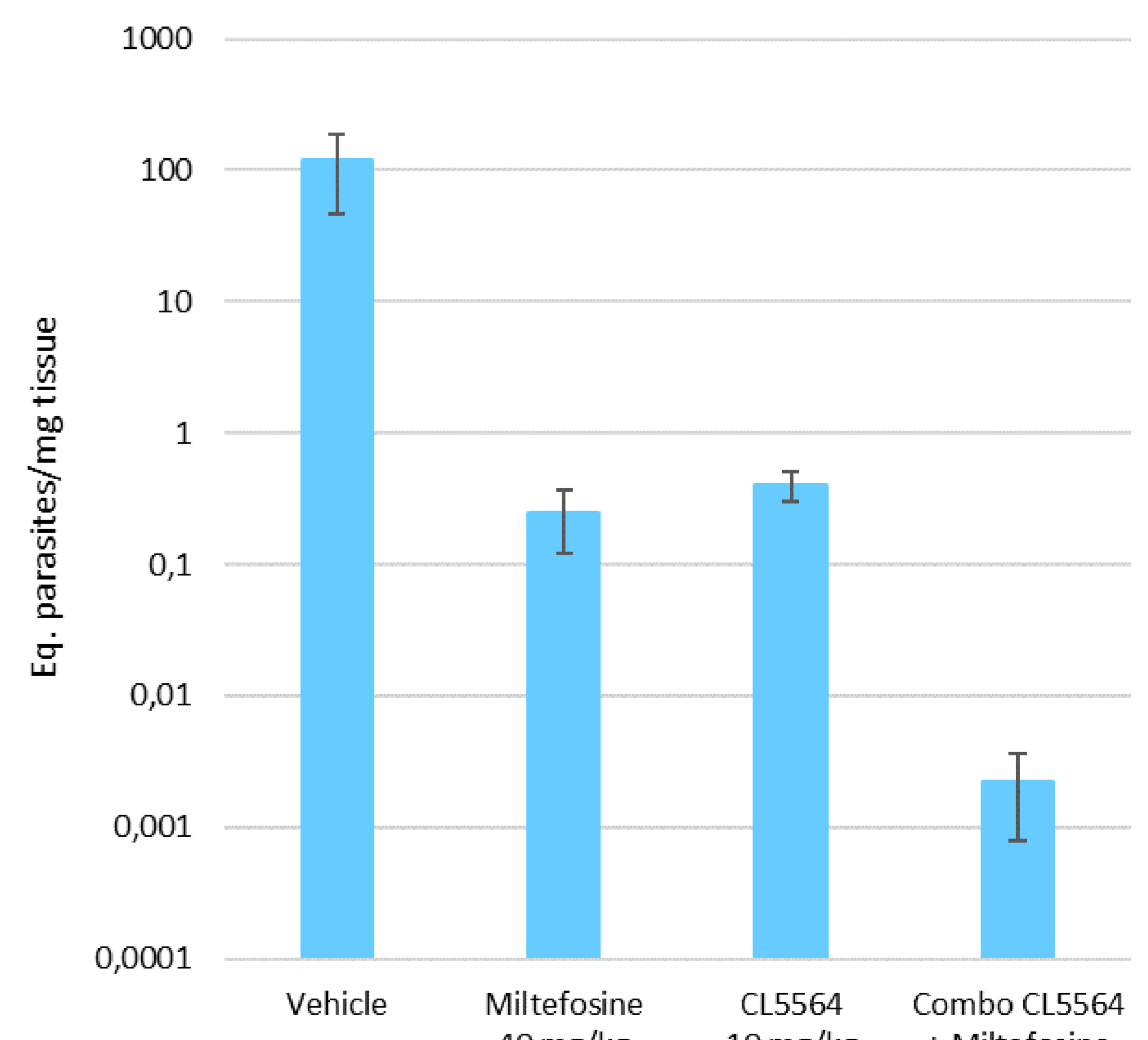
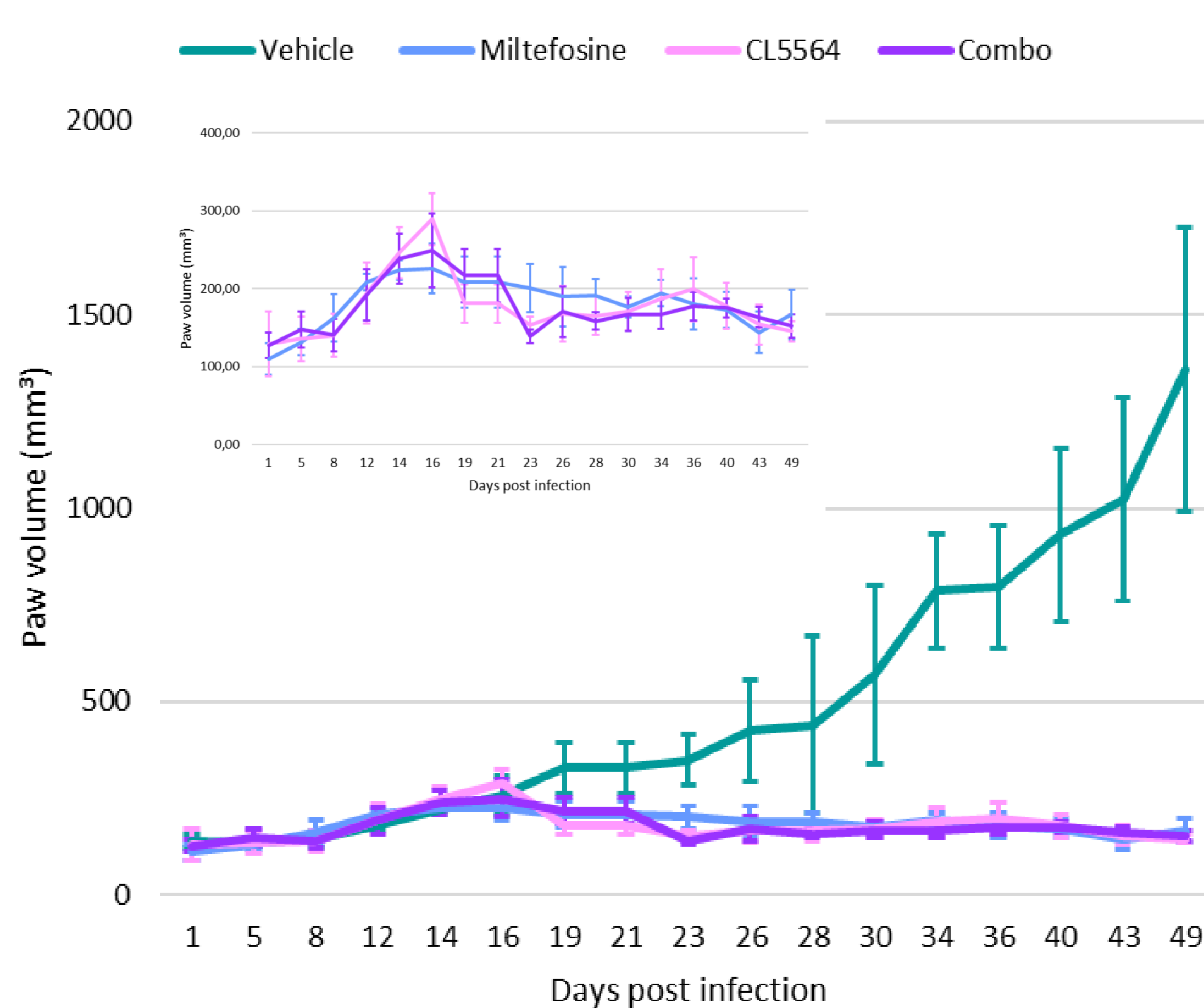
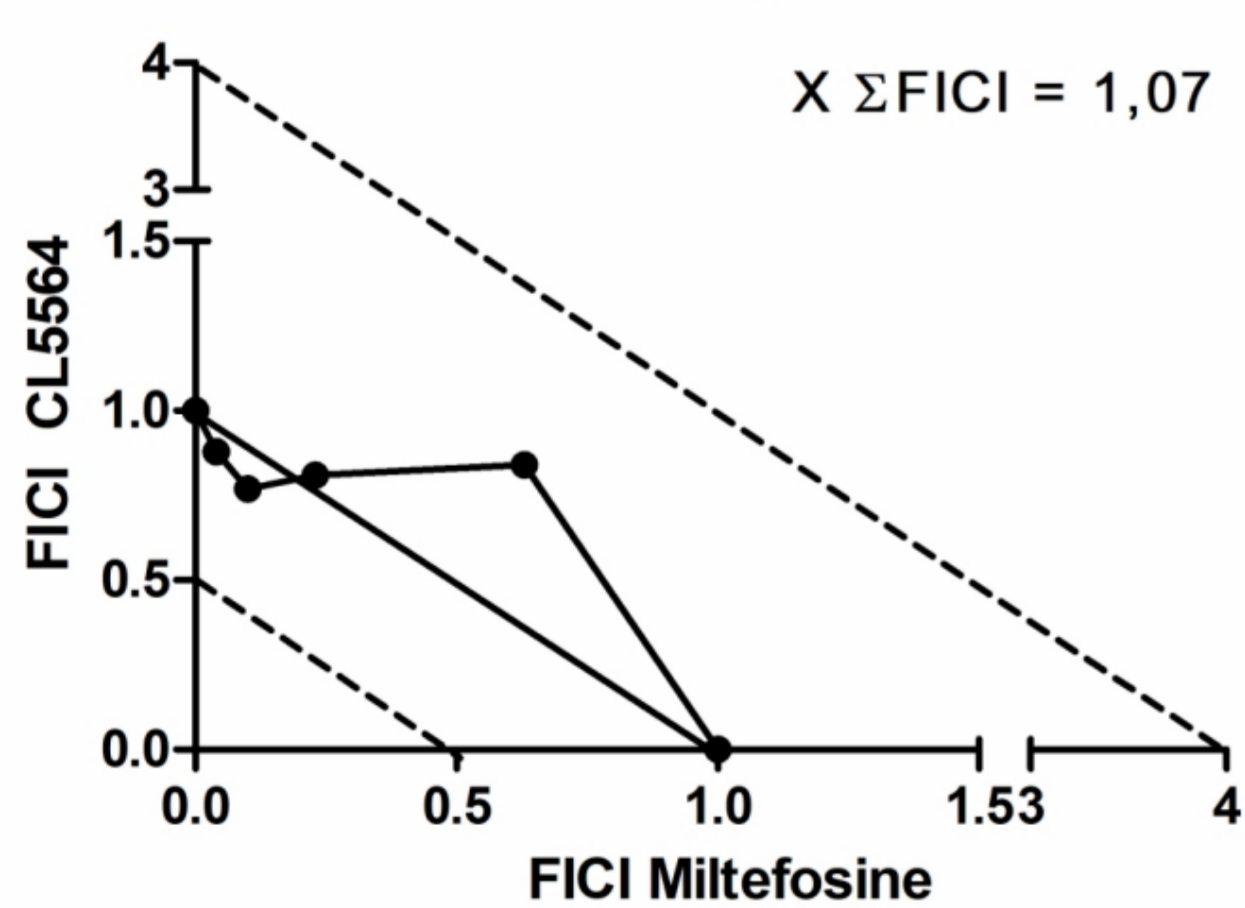
3 No parasites in the cultures of the ML, CL5564 and combo treated mice



2 ML and CL5564 demonstrated an additive effect on ex vivo amastigotes

4 CL5564 alone reduced paw lesion sizes 97-100%, but in combination with ML, it resulted in almost complete lesion reduction reaching >97%

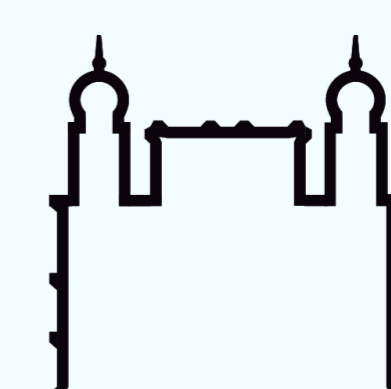
5 CL5564 strongly reduced the parasite load, even more so in combination with ML, the combo ultimately lead to a sterile cure in 2/3 of mice



Want to join us on this journey?



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