

The spiroindolone KAE609 does not induce the development of dormant ring-stages of *Plasmodium falciparum* parasites, *in vitro*

Running Title: KAE609 prevents the growth of artemisinin-arrested ring-stages of *Plasmodium falciparum*

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Supplemental Material

Table S1. Microscopic observations on parasites recovery after exposure of ring-stage parasites of W2 *Plasmodium falciparum* parasites to KAE609, dihydroartemisinin (DHA), artemether (ART), lumefantrine (LUM) and their combinations.

Sample name [Compound xIC ₉₀]	Recrudescence (Yes/No)	Growing parasites observed (days)	No. of days until ~0.5% Parasite mia	No. of experimen ts	Dormant rings observed (Yes/No)	Comments
KAE609 1.25x	-			2	No	Parasites did not stop growing as in W2CTL.
KAE609 2.5x	-			2	No	Parasites did not stop growing as in W2CTL.
KAE609 5x	-			2	No	Parasites did not stop growing as in W2CTL.
KAE609 12.5x	Yes	14	16	3	No	Majority of parasites were killed.
KAE609 25x	Yes	18	23	4	No	Majority of parasites were killed.
KAE609 50x	No			4	No	All parasites were killed. Parasite growth was inhibited for the 8 week duration of the experiment.
KAE609 100x	No			2	No	All parasites were killed. Parasite growth was inhibited for the 8 week duration of the experiment.
KAE609 200x	No			1	No	All parasites were killed. Parasite growth was inhibited for the 8 week duration of the experiment.
DHA	Yes	3	5	4	Yes	Growth arrested and resumed.
DHA+KAE609 1.25x	Yes	3	5	1	Yes	Growth arrested and resumed.
DHA+KAE609 2.5x	Yes	5	7	1	Yes	Growth arrested and resumed.

DHA+KAE609 5x	Yes	5	7	1	Yes	Growth arrested and resumed.
DHA+KAE609 12.5x	Yes	16	18	2	Yes	Growth arrested and resumed.
DHA+KAE609 25x	No			2	Yes	All parasites were killed. Parasite growth was inhibited for the 8 week duration of the experiment.
DHA+KAE609 50x	No			2	Yes	All parasites were killed. Parasite growth was inhibited for the 8 week duration of the experiment.
DHA+LUM 10x	Yes	6	10	1	Yes	Growth arrested and resumed.
DHA+LUM 25x	Yes	16	18	2	Yes	Growth arrested and resumed.
DHA+LUM 50x	No			2	Yes	All parasites were killed. Parasite growth was inhibited for the 8 week duration of the experiment.
DHA+LUM 100x	No			2	Yes	All parasites were killed. Parasite growth was inhibited for the 8 week duration of the experiment.
LUM 10x	-			3	No	Parasites did not stop growing as in W2CTL.
LUM 25x	Yes	10		2	No	Majority of parasites were killed.
LUM 50x	No			2	No	All parasites were killed. Parasite growth was inhibited for the 8 week duration of the experiment.
LUM 100x	No			3	No	All parasites were killed. Parasite growth was inhibited for the 8 week duration of the experiment.
ART 100x	Yes	3	4	3	Yes	Growth arrested and resumed.

ART+LUM 10x	Yes	4	9	1	Yes	Growth arrested and resumed.
ART+LUM 25x	Yes	12	14	2	Yes	Growth arrested and resumed.
ART+LUM 50x	No			2	Yes	All parasites were killed. Parasite growth was inhibited for the 8 week duration of the experiment.
ART+LUM 100x	No			2	Yes	All parasites were killed. Parasite growth was inhibited for the 8 week duration of the experiment.