

Publication

Anti-malarial ozonides OZ439 and OZ609 tested at clinically relevant compound exposure parameters in a novel ring-stage survival assay

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BACKGROUND: Drug efficacy against kelch 13 mutant malaria parasites can be determined in vitro with the ring-stage survival assay (RSA). The conventional assay protocol reflects the exposure profile of dihydroartemisinin. **METHODS:** Taking into account that other anti-malarial peroxides, such as the synthetic ozonides OZ439 (artefenomel) and OZ609, have different pharmacokinetics, the RSA was adjusted to the concentration-time profile of these ozonides in humans and a novel, semi-automated readout was introduced. **RESULTS:** When tested at clinically relevant parameters, it was shown that OZ439 and OZ609 are active against the Plasmodium falciparum clinical isolate Cam3.I(R539T). **CONCLUSION:** If the in vitro RSA does indeed predict the potency of compounds against parasites with increased tolerance to artemisinin and its derivatives, then the herein presented data suggest that following drug-pulses of at least 48 h, OZ439 and OZ609 will be highly potent against kelch 13 mutant isolates, such as P. falciparum Cam3.I(R539T).

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