IMPACT Project
(mdc-STM)

LONG LASTING FORMULATION OF IVERMECTIN IN THE FIGHT AGAINST VECTORS OF MALARIA

INOVEC - Agropolis
February 14th 2023

IMPACT project: Sustained release of Ivermectin to reduce malaria transmission

- **Malaria remains endemic in 84 countries**
  In 2021, 247 million people were infected worldwide, 95% of them in Africa, leading to 619, 000 deaths (WHO World Malaria Report – 2022)

- **Innovative tools are still needed to complement the vector control toolbox**

- **The project IMPACT aims at developing a 3-month long-acting ivermectin for malaria vector control that is safe, high-quality, user-accepted, easy to administer, available and accessible in LMICs at an affordable and cost-effective price**

Unitaid

April 2020 – December 2023

Up to $6.4 million grant
to fund the lead formulation selection and preclinical activities

Ongoing submission preparation to extend funding until end of Ph.I

Research collaboration
with academic centers of excellence

IRD CIRDES IRSS

License agreement to ensure global access

medicines patent pool

IMPACT project: Sustained release of Ivermectin to reduce malaria transmission

Supplementary grant to:

- ❑ **Investigate the presence & pharmacokinetic properties of ivermectin metabolites in cattle plasma samples following a 3-month long-acting ivermectin injection**
- ❑ **Generate data from PK/PD modeling**
- ❑ **Evaluate the mosquitocidal efficacy of the main IVM metabolites against *An.dirus* & *An.minimus* through a membrane-feeding assay**

BILL & MELINDA GATES foundation

2021

Supplementary grant

Funding for analysis of metabolites PK/PD in cattle with MORU

Research collaboration

with academic centers of excellence

MORU Tropical Health Network

&

IRD CIRDES IRSS

BEPO®, the technology behind the 3-month long-acting formulation of Ivermectin

FORMULATION

Customized formulation for each indication

> PEG/PLA polymers

> Hydrophilic solvent

> API

SUBCUTANEOUS OR LOCAL INJECTION

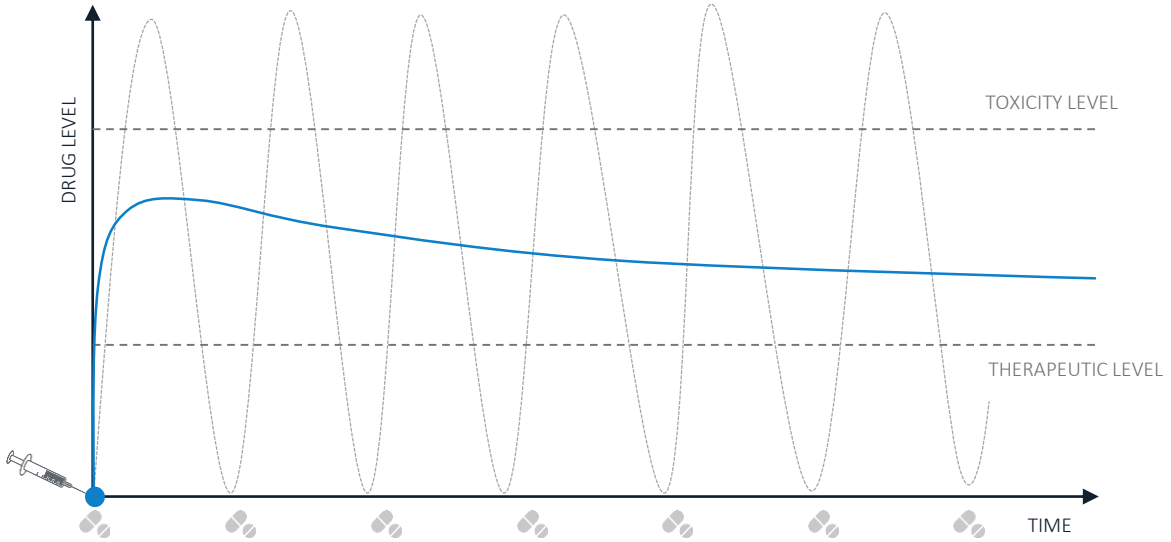
In situ depot precipitates immediately after subcutaneous

CONTROLLED RELEASE

API is released as depot fully degrades

Key features:

- **Single subcutaneous injection**
- **Immediate onset to efficacy**
- **Steady release for month(s)**
- **Bioresorbable**
- **Easy ot handle/inject**



IMPACT project: Efficacy data in field (Burkina Faso)

- **Study design in field**

Per experimental condition:

- **6 Control Cattle**
- **6 Treated cattle at 1.0 mg/kg dose**
- **6 Treated cattle at 1.5 mg/kg dose**

Follow-up: 5 months

Experimental Hut

Two complementary approaches

Place cow in double tent or experimental hut

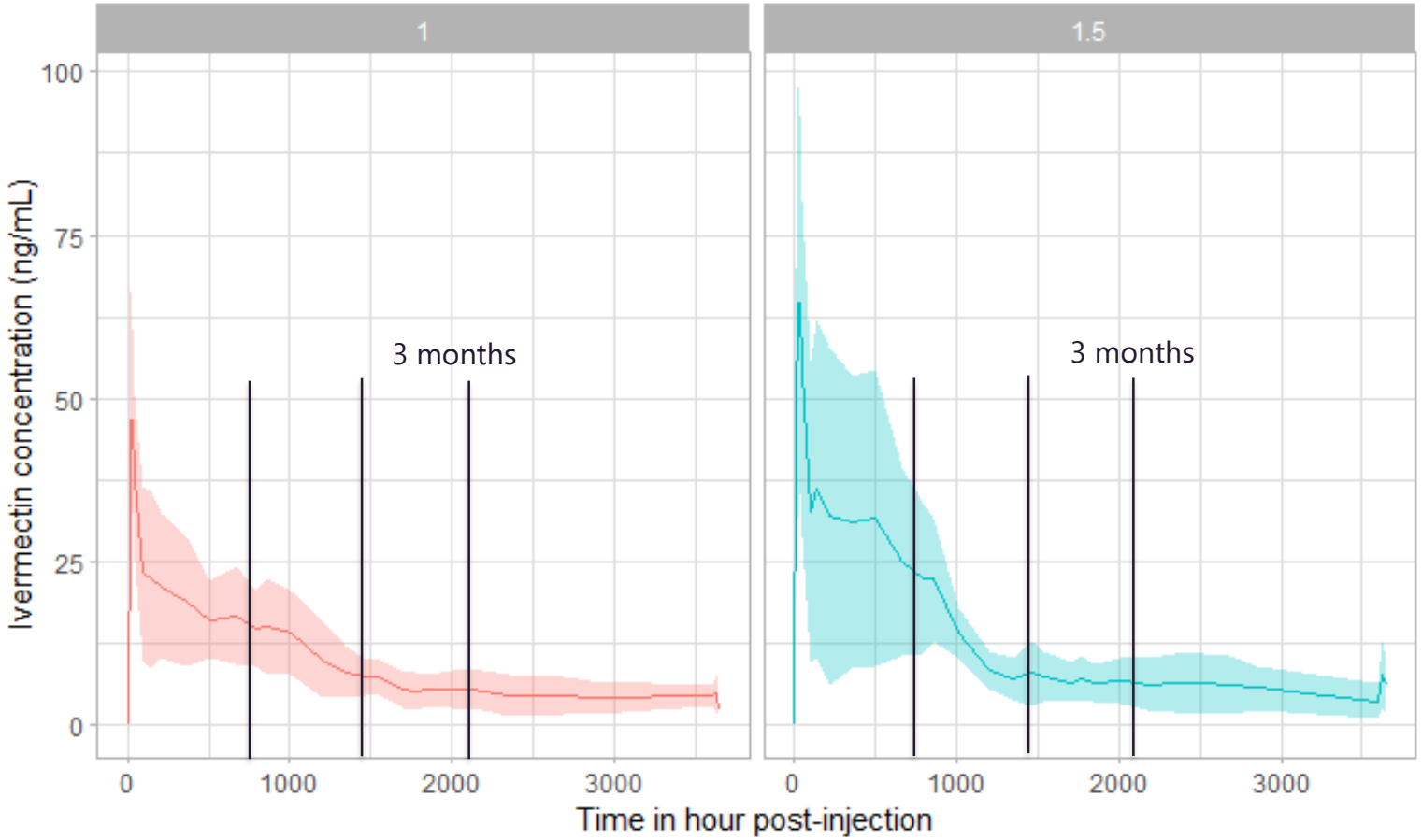
Blood-fed mosquitoes endophageous/ exophageous

Daily monitoring of mortality

Experimental Tent

IMPACT project: Efficacy data in field (Burkina Faso)

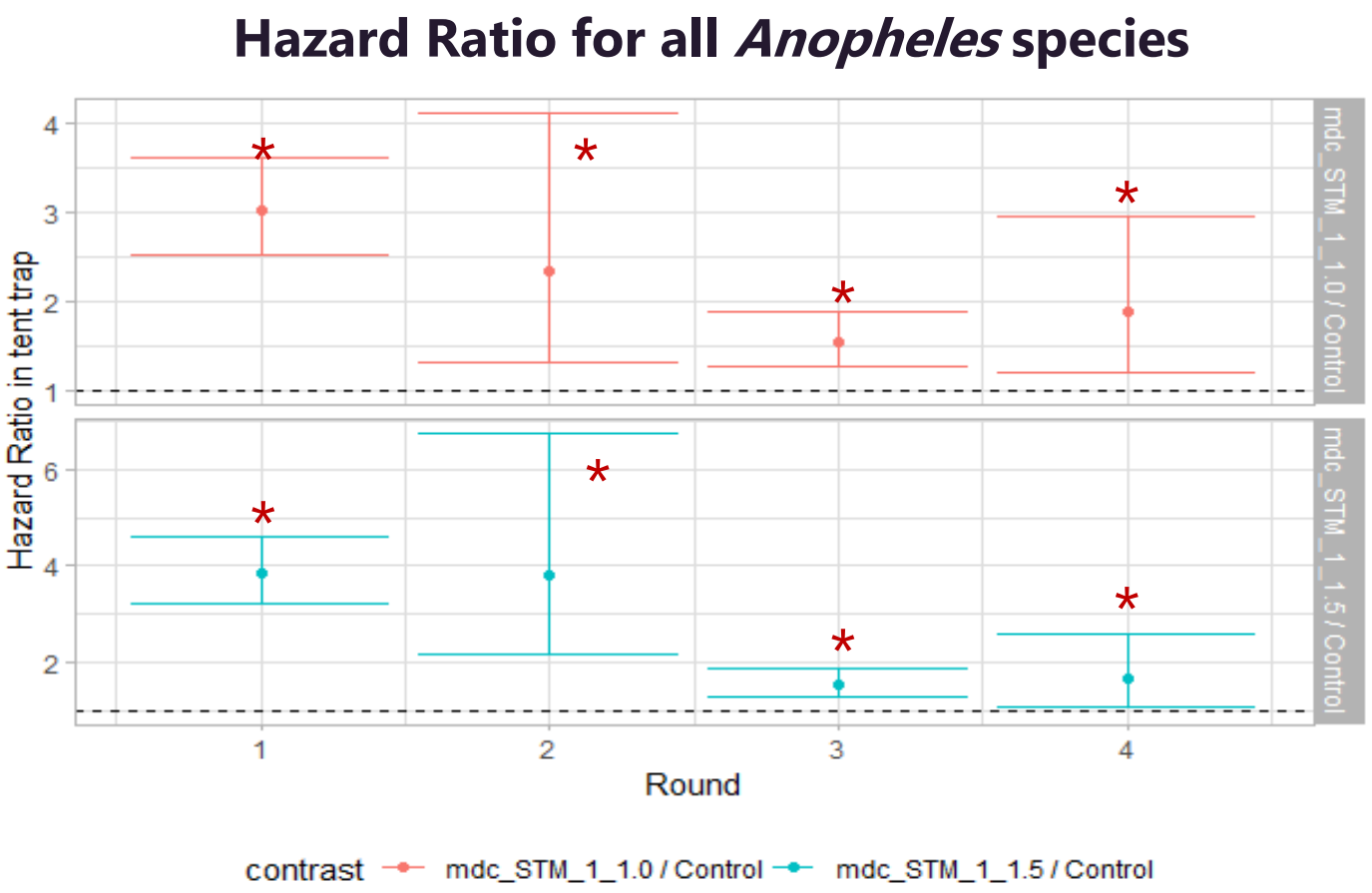
Highlight of the main results (Pharmacokinetics)



The IVM plasma-concentration time profile cattle is consistent with a sustained mosquitocidal efficacy against Anopheline species for 2-3 months

IMPACT project: Efficacy data in field (Burkina Faso)

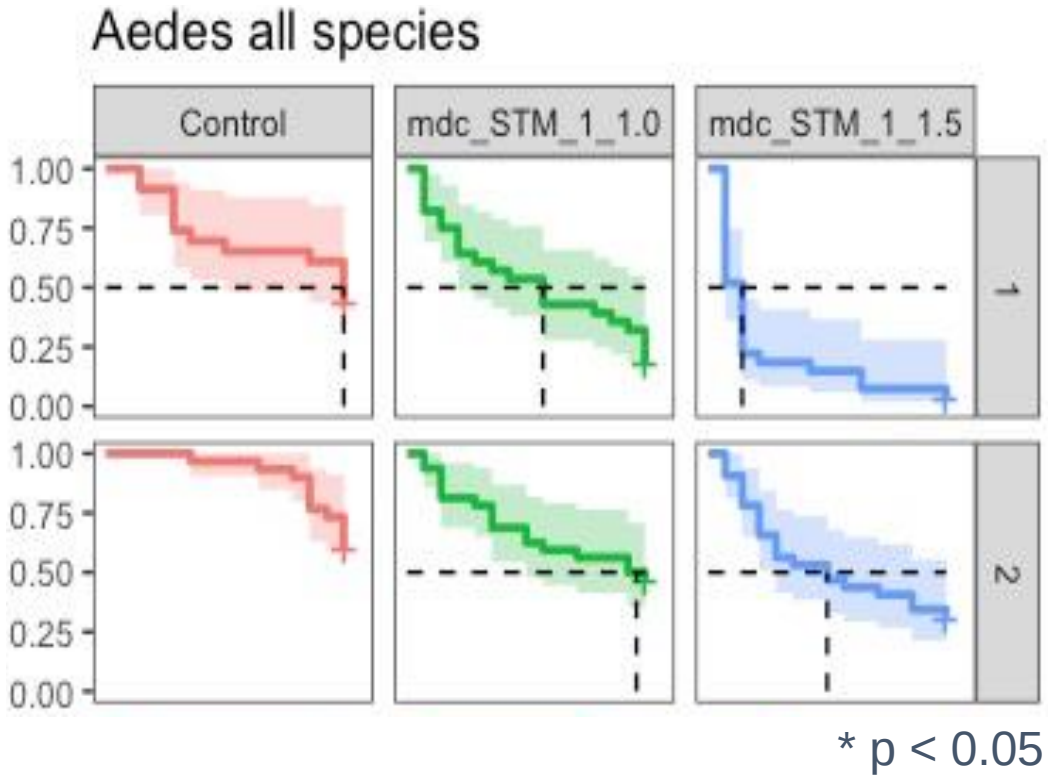
Highlight of the main results (Entomological Efficacy)



Overall, mosquitoes from the Anopheles genus that fed on treated cattle were 2 to 4 times more likely to die compared to the control during the whole experiment (3 months).

Injectable Long-acting ivermectin: Beyond Anopheline species

Collateral effect on Aedes species



→ 1 wk post-injection

*

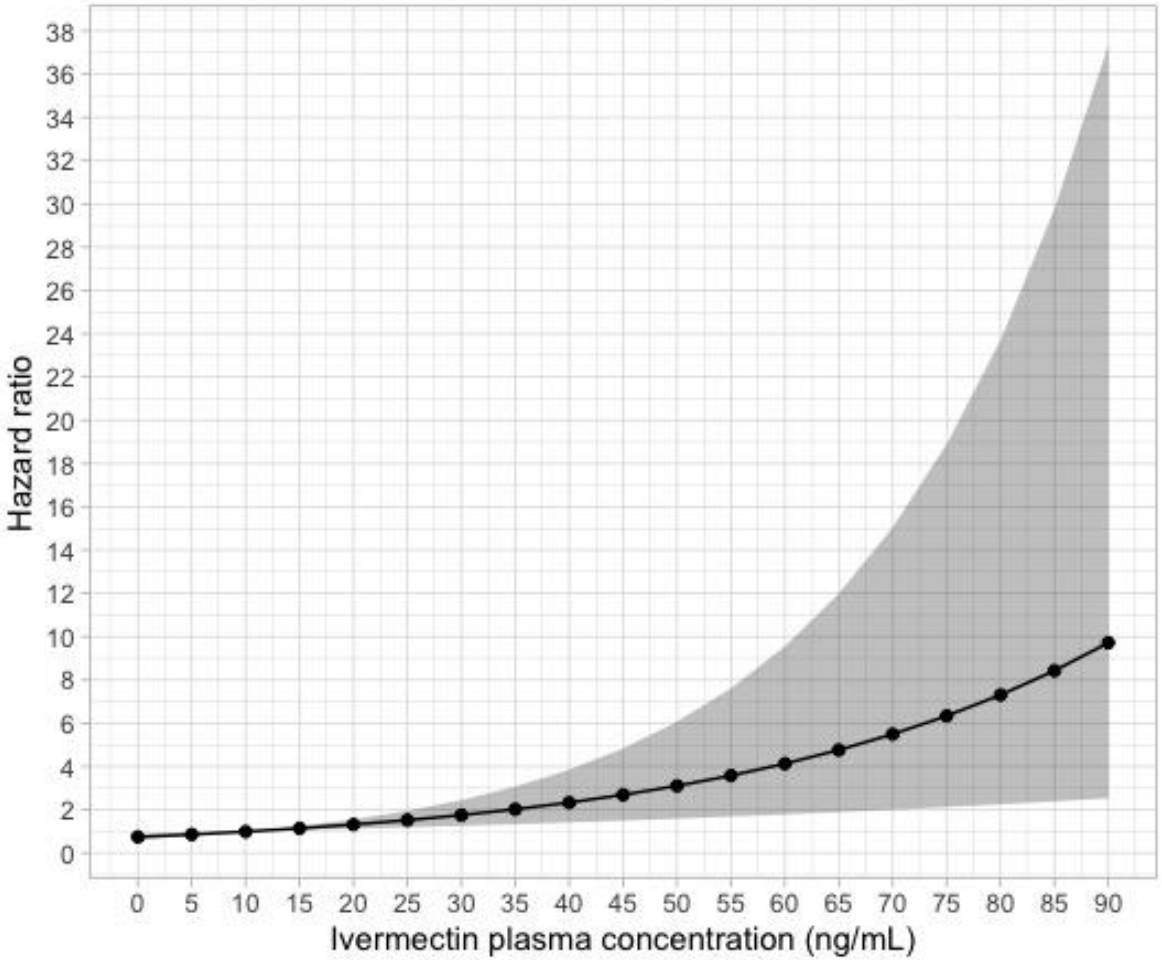
→ 4 wks post-injection

* p < 0.05

The risk of mortality is significantly increased compared to control for the formulation dose 1.5 mg/kg (p value < 0.05). An Aedes mosquitoe exposed to 1.5 dose has 7 times higher risk to death 1 week post-injection and 3 times higher 1 month post-injection

Injectable Long-acting ivermectin: Beyond Anopheline species

Collateral effect on Aedes species



Hazard Ratio estimated from cox model in function of IVM concentration (in ng/mL). A significant effect on Aedes mortality risk is estimated from a cattle plasma concentration of 20ng/mL.