The “Development of Triple Artemisinin-based Combination Therapies (DeTACT)” project

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Artemisinin-based Combination Therapy (ACT)

- Artemether-lumefantrine
- Artesunate-mefloquine
- Dihydroartemisinin-piperaquine
- Artesunate-amodiaquine
- Artesunate-sulphadoxine-pyrimethamine
- Artesunate-pyronaridine
Artemisinin resistance presents as slower clearance
ACTs are failing in Southeast Asia

Global spread of multidrug-resistant parasites could derail malaria elimination efforts and reverse all recent gains in malaria control
Artemisinin Molecular Surveyor
Artemisinin resistance in Africa

Emergence and clonal expansion of in vitro artemisinin-resistant *Plasmodium falciparum* kelch13 R561H mutant parasites in Rwanda


Evidence of Artemisinin-Resistant Malaria in Africa

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If TACTs are safe, well tolerated, and efficacious, they can be deployed very quickly

van der Pluijm et al, Trends Parasitol 2021
TRACII clinical trial is proof of concept of TACTs

- 1100 patients recruited
- Uncomplicated falciparum malaria with asexual parasite density of 5,000 to 200,000/µL
- Median age 23y (78% male)
- TACTs: AL+AQ and DHA-PPQ+MQ
- D42 PCR-corrected efficacy >90% for TACTs
- Safe and well-tolerated

van der Pluijm et al, Lancet 2020
DeTACT project
Development of Triple Artemisinin Combination Therapies

- Drug development
- Clinical trial
- Mathematical modelling
- Bioethics
- Market positioning
- Communications

DeTACT 1st Investigators’ Meeting, Thailand, Jan 2019
DeTACT project
Development of Triple Artemisinin Combination Therapies

- **Drug development**: Produce a co-packaged presentation of two Triple Artemisinin-based Combination Therapies (TACTs)

- **Artemether-lumefantrine + amodiaquine/placebo**
  (AL+AQ/placebo)
  *Fosun Pharma, China*

- **Artesunate-mefloquine + piperaquine/placebo**
  (AS+MQ+PPQ/placebo)
  *Bilcare Research, India*

Fosun Pharma have developed **ALAQ Fixed Dose Combination** as part of their corporate social responsibility.
DeTACT project
Development of Triple Artemisinin Combination Therapies

- Clinical trial: Randomised, partially-blinded, placebo-controlled clinical trial with TACTs and ACTs+placebo (n=3468) – for safety, tolerability and efficacy

2476 enrolled by 25 Sept 2023
Complete enrollment by Dec 2023
DeTACT project
Development of Triple Artemisininin Combination Therapies

- Mathematical modelling – Health and economic benefits of deploying TACTs in countries with different first-line therapies, transmission intensities etc.

Settings:

**ACTs**: AL, DHA-PPQ, ASAQ

**TACTs**: AL+AQ, ASMQ+PPQ

**PfPR (%)**: 0.1, 1.0, 10

**Coverage (%)**: 25, 50, 70

Total of 54 comparisons (27 comparisons per TACT)

Triple ACTs may delay artemisininin resistance and decrease treatment failures over 10 years

Nguyen et al, Nature Communications 2023
DeTACT project
Development of Triple Artemisinin Combination Therapies

Bioethics & Market Positioning

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MORU
Paulina Tindana
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Jean-Bosco Ouédraogo
INSTech
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CEMTROD
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Ethical considerations in deploying triple artemisinin-based combination therapies for malaria: An analysis of stakeholders’ perspectives in Burkina Faso and Nigeria

To what extent are the antimalarial markets in African countries ready for a transition to triple artemisinin-based combination therapies?

PLOS ONE

(Conducted prior to confirmation of artemisinin resistance in Rwanda, Uganda)
DeTACT project
Development of Triple Artemisinin Combination Therapies

- Communication – Communicate findings to stakeholders and raise awareness
FD-TACT project (expected to begin in 2024)

Fixed dose combination (FDC) of artemether-lumefantrine-amodiaquine (ALAQ)

- ALAQ FDC – development
- ALAQ FDC – clinical trial
- ALAQ FDC – prequalification
- ALAQ FDC – commercialization
- Human rights and health equity

DeTACT project

- Drug development
- Clinical trial
- Mathematical modelling
- Bioethics
- Market positioning

Extension:
ALAQ deployment readiness in Rwanda & Uganda
- Communications
- Individual patient data meta-analysis

MORU Tropical Health Network

- Wellcome
- Swedish University
- University of Oxford