



# DeTACT

## Development of Triple Artemisinin-based Combination Therapies

DeTACT Project Investigators

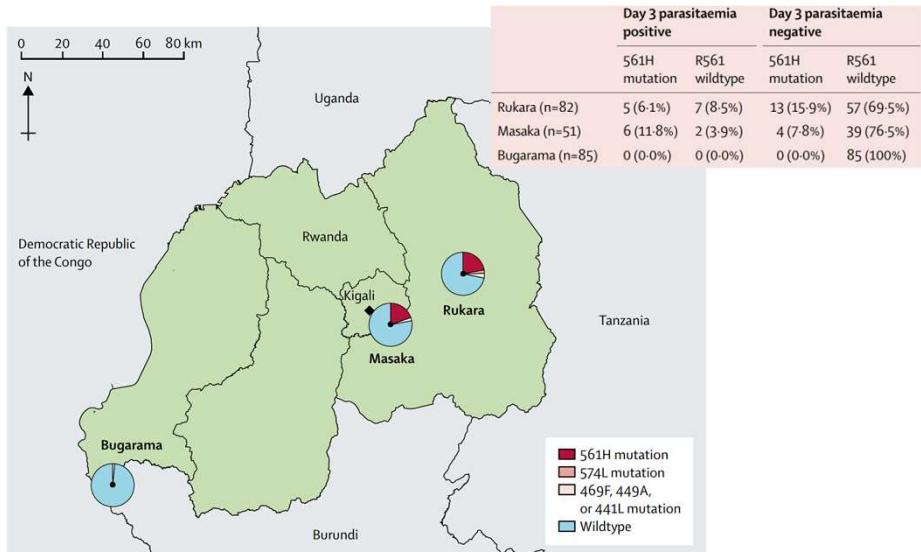
Presenter: Mehul Dhorda, PhD

Mahidol-Oxford Tropical Medicine Research Unit

SMC Alliance Meeting  
Conakry, 28 Feb – 02 Mar 2023

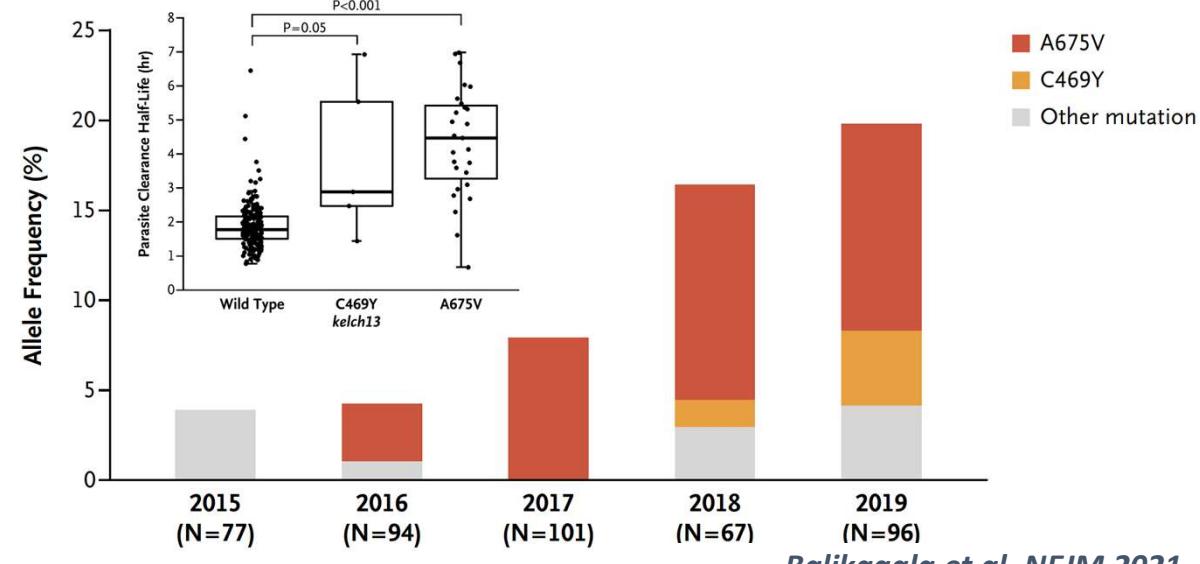


# Artemisinin partial resistance in East Africa



*Uwimana et al. LID 2021*

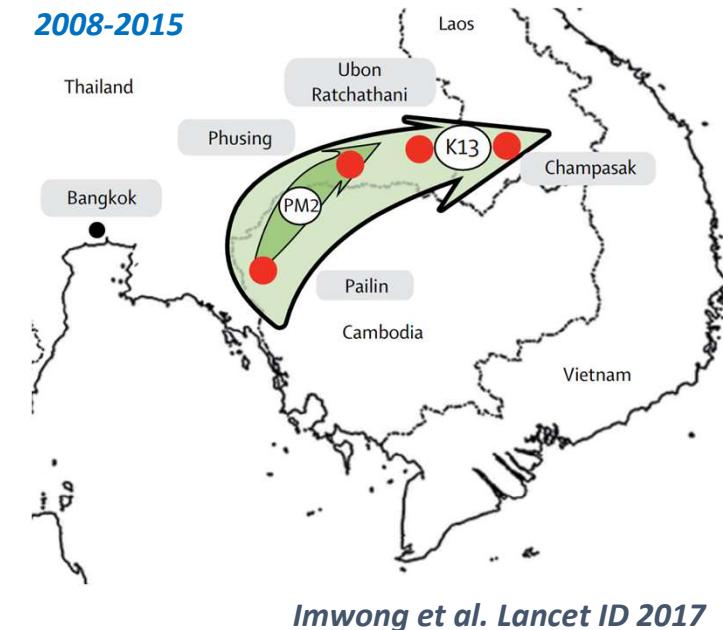
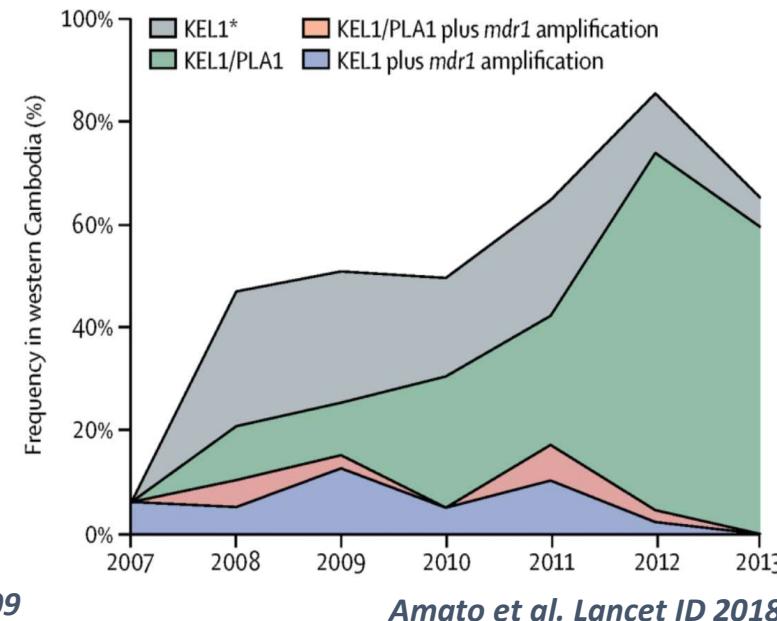
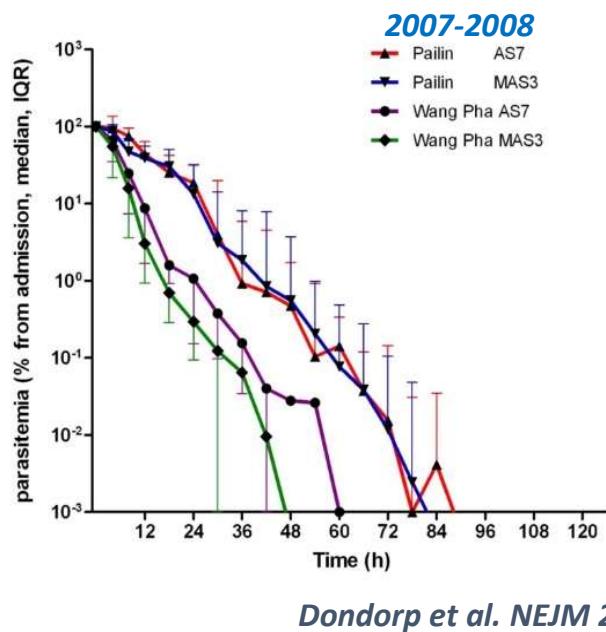
*Rwanda*



*Balikagala et al. NEJM 2021*

*Uganda*

# Artemisinin partial resistance – spread in the Greater Mekong Subregion

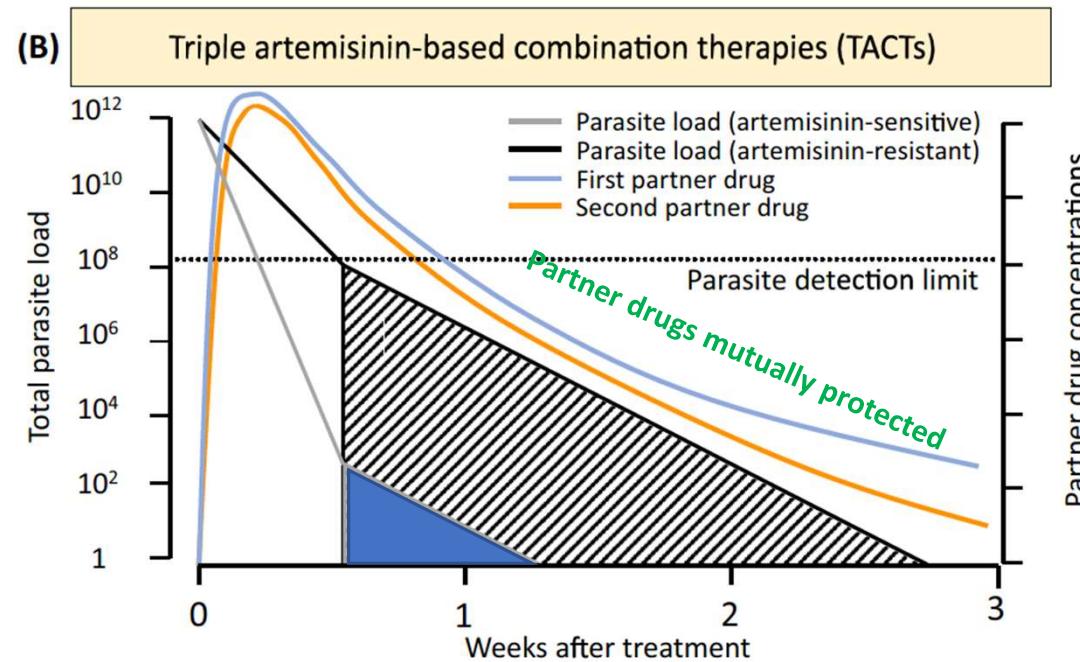
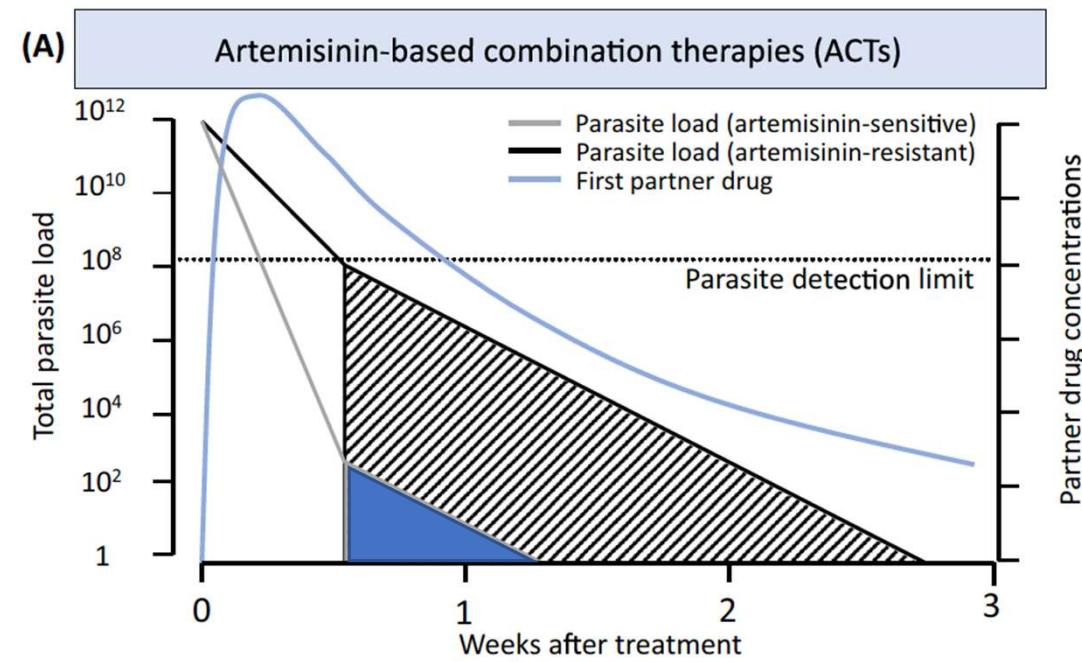


Western Cambodia

Cambodia

Greater Mekong Subregion

# Triple ACTs – "enhanced" ACTs



*Considerations for choosing TACT partner drugs:*  
**Resistance mechanism**  
**Pharmacokinetic profile**

# Triple ACT – 'TRACII' & 'TACT-CV' studies



Triple artemisinin-based combination therapies versus artemisinin-based combination therapies for uncomplicated *Plasmodium falciparum* malaria: a multicentre, open-label, randomised clinical trial  
*van der Pluijm et al. Lancet 2020*

BILL & MELINDA GATES foundation

Triple therapy with artemether-lumefantrine plus amodiaquine versus artemether-lumefantrine alone for artemisinin-resistant, uncomplicated falciparum malaria: an open-label, randomised, multicen  
*Peto et al. LID 2022*

## Efficacy

- ***Efficacy of DHA-PPQ+MQ >> efficacy of DHA-PPQ in Cambodia, Thailand, Vietnam (sites with ART-R + PIP-R)***
- Similar efficacy of TACT (AL+AQ, DP+MQ) versus ACT (AL, ASMQ)

## Innocuité/tolérabilité

- In general, comparable to ACTs
- Mild but significant increase in vomiting (but comparable/lower than ASAQ)
- Mild to moderate and transient increase in bradycardia, creatinine levels with AL+QA vs AL

# DeTACT Project

## Development of Triple Artemisinin-based Combination Therapies

- Product Development
- Clinical trial
- Mathematical modeling
- Bioethics
- Market positioning



# DeTACT – Bioethics and Market Positioning



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Olugbenga Mokuolu  
CEMTROD



Freek de Haan  
University of Utrecht



Ellen Moors  
University of Utrecht



Wouter Boon



Deploying triple artemisinin-based combination therapy (TACT) for malaria treatment in Africa: ethical and practical considerations

Paulina Tindana<sup>1</sup>, Freek de Haan<sup>2</sup>, Chanaki Amaratunga<sup>3,4</sup>, Mehul Dhorda<sup>3,4</sup>, Rob W. van der Pluijm<sup>3,4</sup>, Arjen M. Dondorp<sup>3,4</sup> and Phaik Yeong Cheah<sup>3,4\*</sup>

Malaria Journal

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

Freek de Haan<sup>1</sup>\*, Oladimeji Akeem Bolarinwa<sup>2</sup>, Rosemonde Guissou<sup>3</sup>, Fatoumata Tou<sup>4</sup>, Paulina Tindana<sup>5</sup>, Wouter P. C. Boon<sup>1</sup>, Ellen H. M. Moors<sup>1</sup>, Phaik Yeong Cheah<sup>3,4</sup>, Mehul Dhorda<sup>6,7</sup>, Arjen M. Dondorp<sup>6,7</sup>, Jean Bosco Ouédraogo<sup>3,4</sup>, Olugbenga A. Mokuolu<sup>2</sup>, Chanaki Amaratunga<sup>6,7</sup>

PLOS ONE

**MORU**  
Tropical Health Network

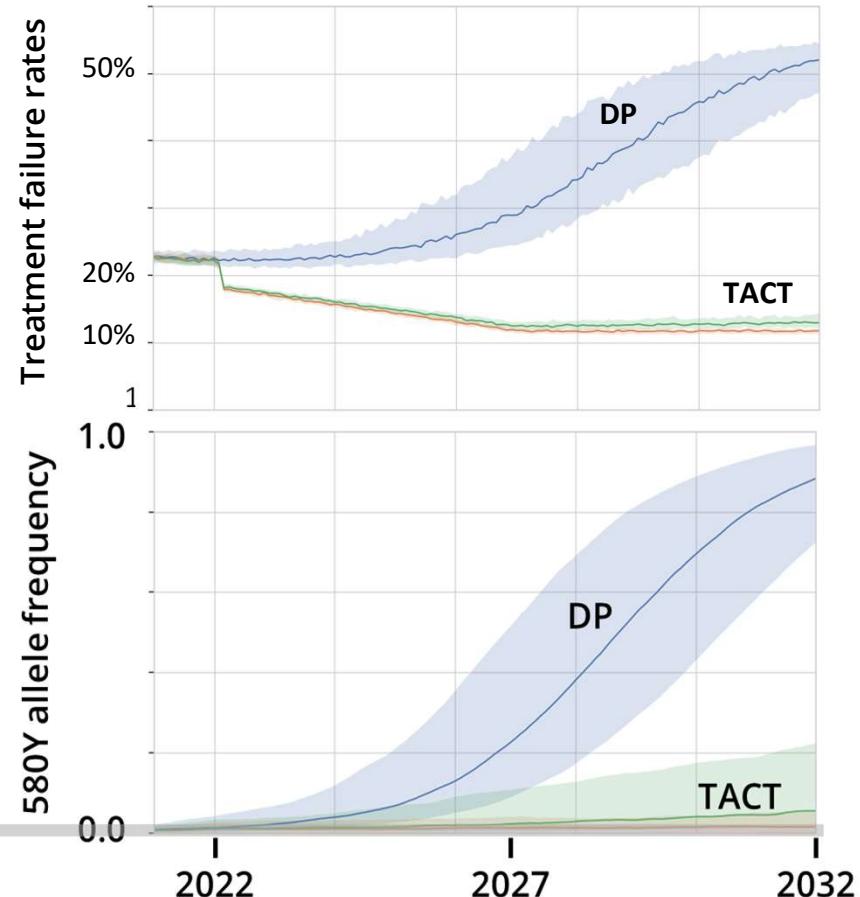
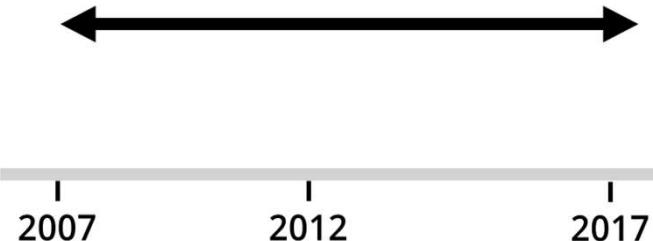
*(Studies conducted prior to confirmation of partial artemisinin resistance in Rwanda, Uganda)*

[www.tropmedres.ac](http://www.tropmedres.ac)

# DeTACT – Modelling studies

- TACT may delay artemisinin resistance and decrease treatment failures over 10 years
- Switching to TACT – the sooner the better
- Phasing out TACT is not desirable

15 years of DHA-PPQ  
as first-line therapy



Maciej Boni  
PSU



Ricardo Aguias  
MORU

# DeTACT – Clinical Trial

**Africa**  
 B. Faso  
 DRC  
 Gambia  
 Guinea  
 Niger  
 Nigeria  
 Rwanda  
 Tanzania



~3000  
Patients

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



Fixed-Dose Combination in development

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



# Interim Analysis: Trends Identified

- **Cardiotoxicity:** Increased bradycardia with AL-AQ (but clinically non-significant)
- **Vomiting:** More patients treated with TACT vomited (but less vomiting than ASAQ)
- **Anemia:** Similar for "matched" TACT-ACT pairs, lower in AS-MQ-based treatments
- **Neutropenia:** Less common with TACT
- **Hepatic and renal parameters:** Comparable across all trial arms

# Prospects

- **Clinical studies**
- DeTACT: Results expected at the end of 2023
  - FD-TACT: Planning phase, results expected at the end of 2024?
  - **Regulatory submissions planned for 2025**
- **Cost**
- To be confirmed
  - More than AL but most likely cheaper than other ACTs

# Thank you!

INSTech, Burkina Faso

KIMORU, DRC

MRC, Gambia

CNFRSR, Guinea

Epicentre, Niger

CEMTROD, Nigeria

University of Rwanda

NIMR-Tanga, Tanzania

Dev Care Foundation, Bangladesh

CNM, Cambodia

EOCRU, Indonesia

MORU CTSG Teams



University of Ghana

Utrecht University

Penn State University

FTM, Mahidol University

Tridem Pharma / Fosun

MMV

FHI Clinical

WWARN

DeTACT DSMB

DeTACT Project Steering  
Committee

Trial participants,  
their parents/guardians



Chanaki Amaratunga  
DeTACT Coordinator  
MORU



Arjen Dondorp  
Principal Investigator  
MORU

[www.tropmedres.ac](http://www.tropmedres.ac)

