

DeTACT

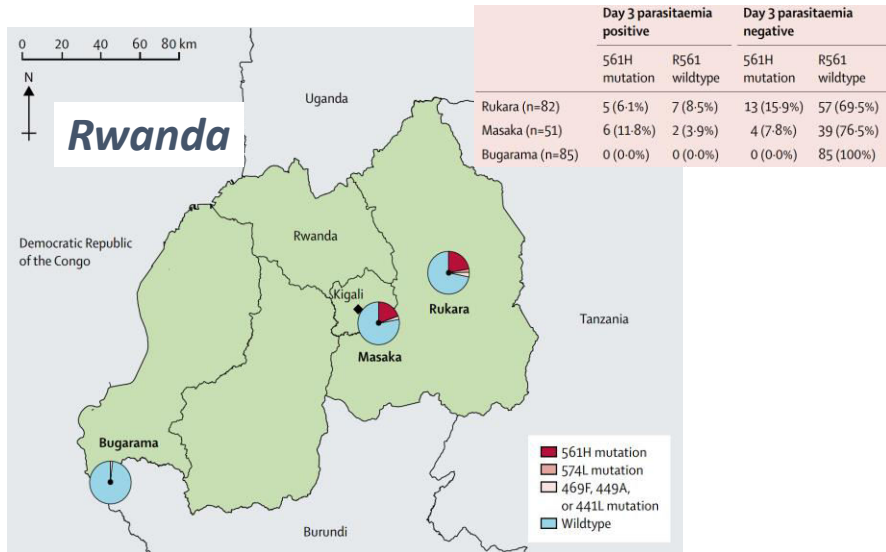
Development of

Triple Artemisinin-based Combination Therapies

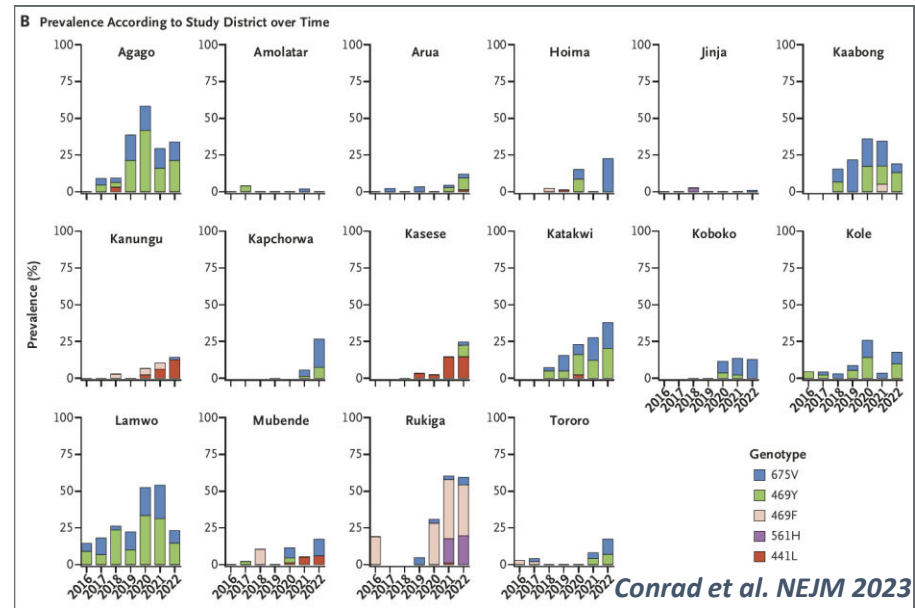
Mahidol-Oxford Tropical Medicine Research Unit
DeTACT Project Investigators

RBM Case Management Working Group Meeting
Kigali, Rwanda
24-26 Sep 2024

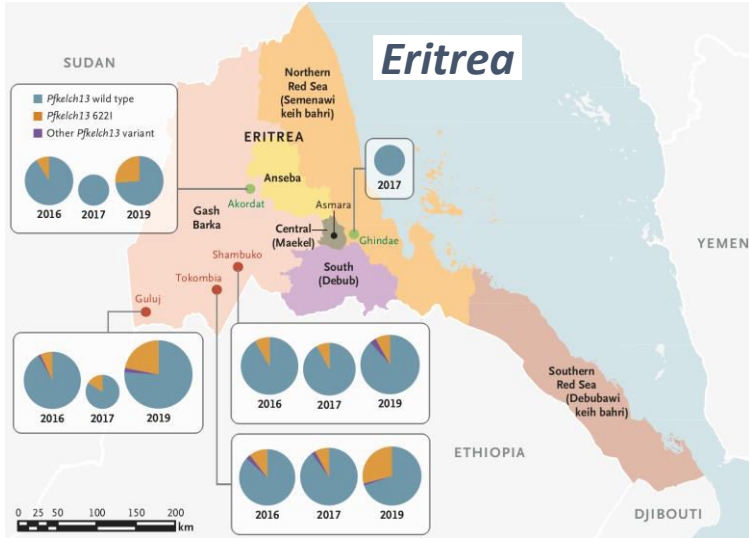
ART-R (Artemisinin partial resistance) in Africa



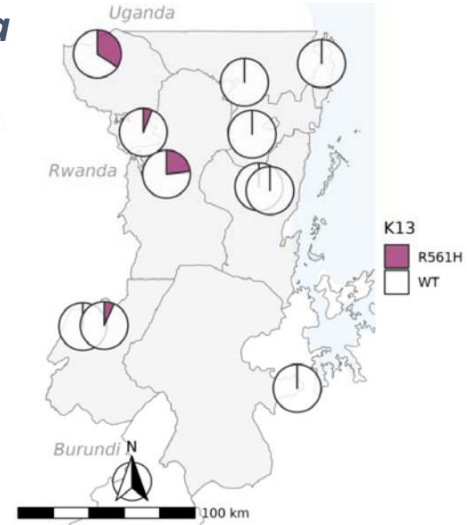
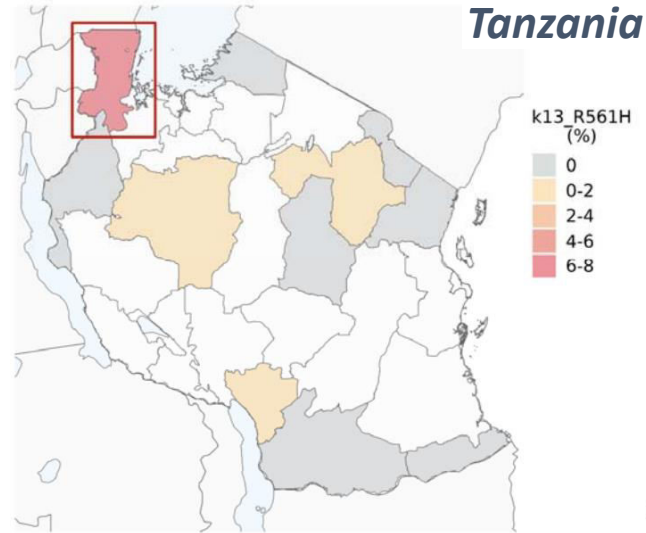
Uwimana et al. LID 2021



ART-R in Africa

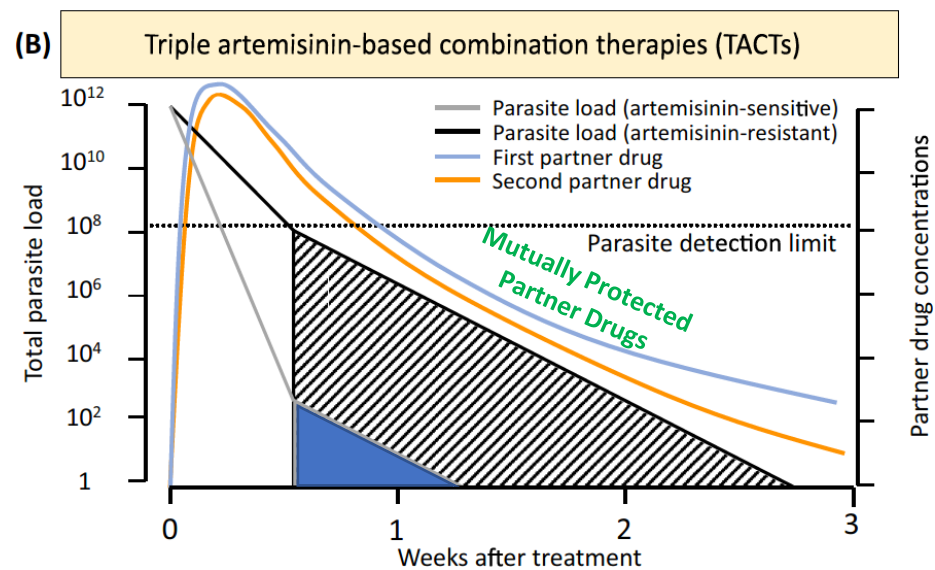
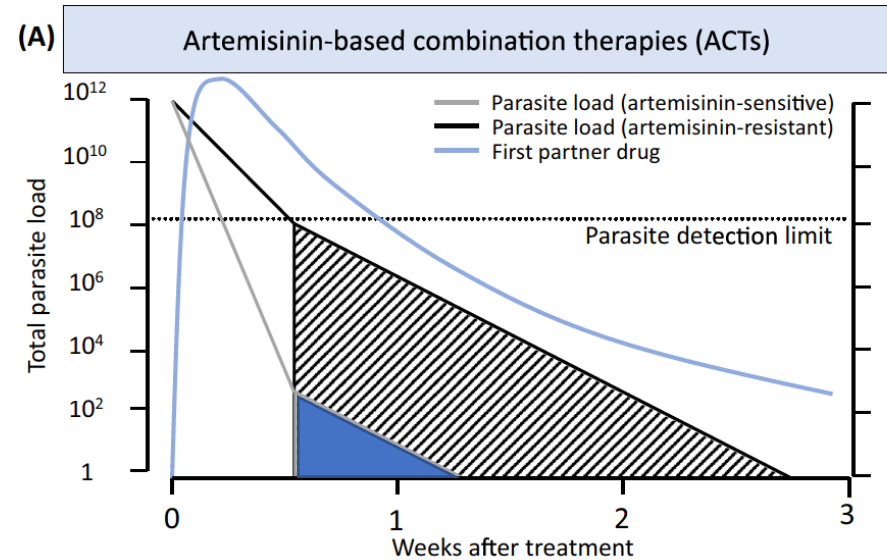


Mihreteab et al. NEJM 2023



Juliano et al. 2023 (pre-print, medRxiv)

Triple ACTs = "Enhanced" ACTs



Considerations for choosing TACT partner drugs:

Mechanism of resistance

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*



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

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

Safety/Tolerability

- In general, comparable to ACTs
- Slight but significant increase in vomiting (but comparable/below ASMQ)
- Mild to moderate and transient increase in bradycardia, serum creatinine with AL+AQ vs AL

DeTACT project

Development of Triple Artemisinin-based Combination Therapies



- Product Development
- Clinical Trial
- Bioethics
- Market study
- Mathematical Modeling
- Individual Patient Data Meta-analysis



DeTACT – Bioethics and Market Research



Phaik Yeong Cheah
MORU



Paulina Tindana
University of Ghana



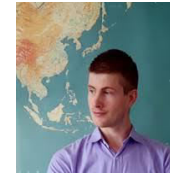
Jean-Bosco Ouédraogo
INSTech



Olugbenga Mokuolu
CEMTRD



Freek de Haan



Ellen Moors
University of Utrecht



Wouter Boon



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

Paulina Tindana¹, Freek de Haan², Chanaki Amaratunga^{3,4}, Mehul Dhorda^{3,4}, Rob W. van der Pluijm^{3,4}, Arjen M. Dondorp^{3,4} and Phaik Yeong Cheah^{3,4*}

Malaria Journal

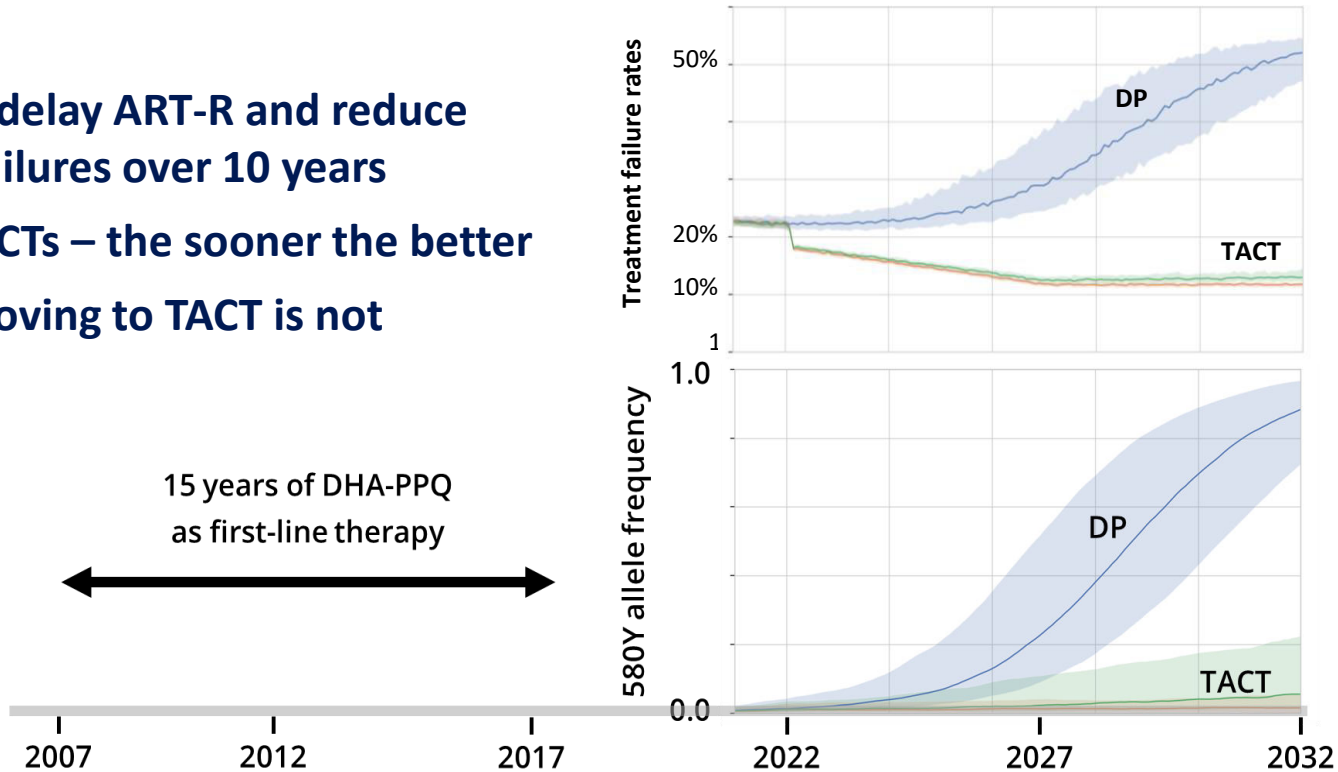
To what extent are the antimalarial markets in African countries ready for a transition to triple artemisinin-based combination therapies?

Freek de Haan^{1*}, Oladimeji Akeem Bolarinwa², Rosemonde Guissou³, Fatoumata Tou⁴, Paulina Tindana⁵, Wouter P. C. Boon¹, Ellen H. M. Moors¹, Phaik Yeong Cheah^{6,7}, Mehul Dhorda^{6,7}, Arjen M. Dondorp^{6,7}, Jean Bosco Ouedraogo^{3,4}, Olugbenga A. Mokuolu², Chanaki Amaratunga^{6,7}

PLOS ONE

DeTACT – Modelling Studies

- TACTs could delay ART-R and reduce treatment failures over 10 years
- Switch to TACTs – the sooner the better
- Gradually moving to TACT is not desirable



Maciej Boni
PSU



Ricardo Aguas
MORU

Modelling Study – Rwanda



Robert Zupko
PSU

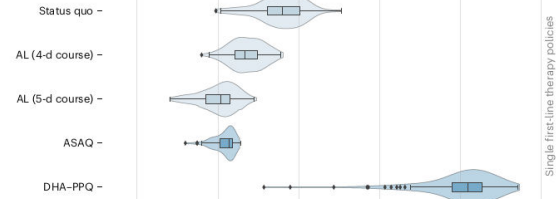
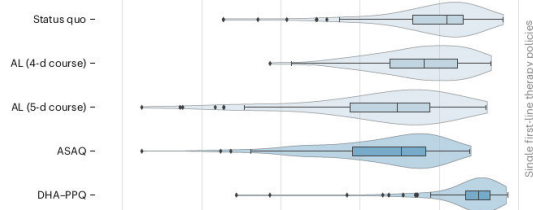


Aline Uwimana
RBC, Rwanda

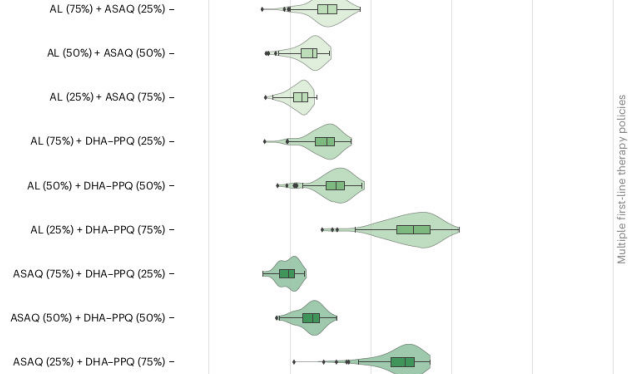
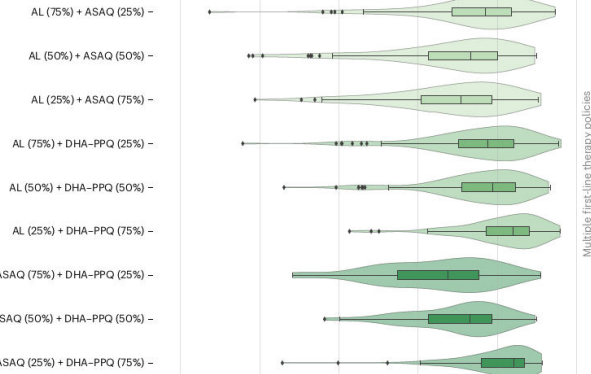


Maciej Boni
PSU

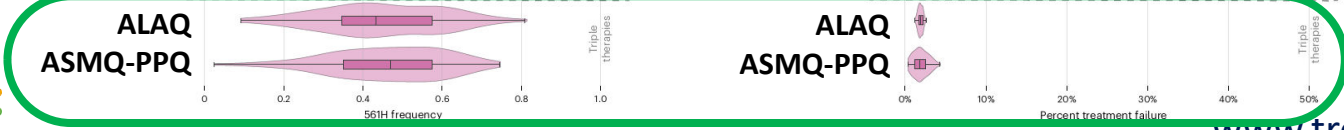
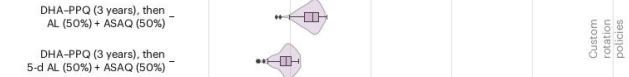
Single ACT (includes 4, 5-day AL)



Multiple First-line Treatment



Rotation



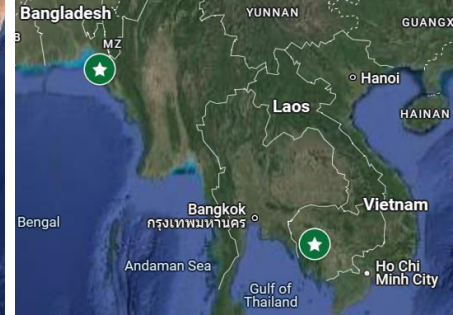
DeTACT – Clinical Trials



Africa
B. Faso
DRC
Gambia
Guinea
Niger
Nigeria
Rwanda
Tanzania



Asia
Bangladesh
Cambodia



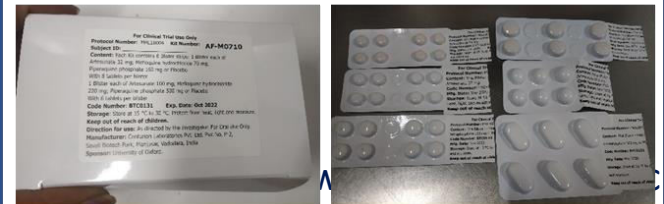
2686
Patients

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

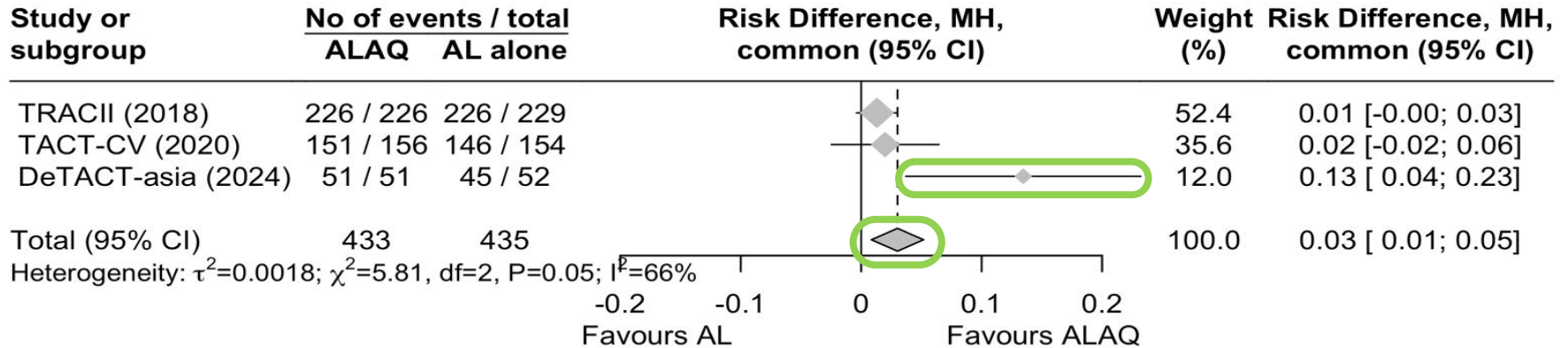


Fixed-Dose Combination in development

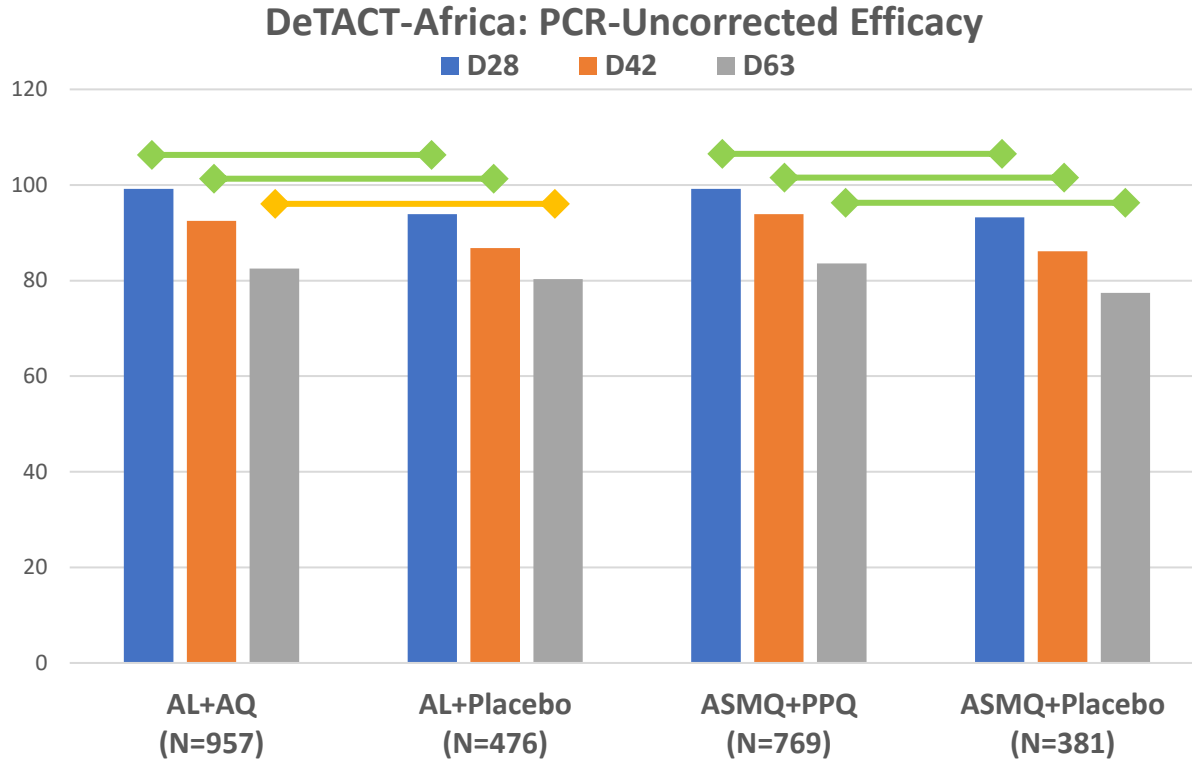
**Artesunate-mefloquine +
 piperazine/placebo
 (AS+MQ+PPQ/placebo)**
Bilcare Research, India



DeTACT Asia: Efficacy



DeTACT Africa: Trends identified – Efficacy



DeTACT: Trends identified – Safety

- **Vomiting:** More patients treated with TACT vomited (but less vomiting than with ASAQ)
- **Cardiotoxicity:** Increased bradycardia with AL-AQ (but clinically non-significant)
- **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 arms

Next steps

- **Clinical trials**
 - DeTACT: Final analyses ongoing
 - FD-TACT: fixed-dose combination of ALAQ, results end-2025
- **Regulatory submissions planned in 2026-27**
- **Cost**
 - To be confirmed
 - More than AL but very likely lower than other ACTs
- **Means to protect lumefantrine**

Merci!

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

MORU 
Tropical Health Network

University of Ghana

Utrecht University

Penn State University

FTM, Mahidol University

Fosun Pharma

MMV

FHI Clinical

WWARN

DeTACT DSMB

DeTACT Project Steering
Committee

Trial participants, their parents/guardians



Chanaki Amaratunga
DeTACT Coordinator
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www.tropmedres.ac

