DeTACT
Development of Triple Artemisinin-based Combination Therapies

DeTACT Project Investigators
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SMC Alliance Meeting
Conakry, 28 Feb – 02 Mar 2023
Artemisinin partial resistance in East Africa

Uwimana et al. LID 2021

Rwanda

Uganda

Balikagala et al. NEJM 2021

www.tropmedres.ac
Artemisinin partial resistance – spread in the Greater Mekong Subregion

2007-2008

Dondorp et al. NEJM 2009

2008-2015

Imwong et al. Lancet ID 2017

Western Cambodia

Cambodia

Greater Mekong Subregion
Triple ACTs – "enhanced" ACTs

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

van der Pluijm et al. TrP 2020
Triple ACT – 'TRACII' & 'TACT-CV' studies

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

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Malaria Journal

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

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(Studies conducted prior to confirmation of partial artemisinin resistance in Rwanda, Uganda)
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
DeTACT – Clinical Trial

~3000 Patients

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

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

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