The potential contribution of tafenoquine to radical cure in vivax malaria elimination

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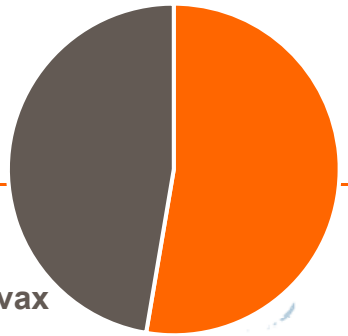
- Everybody who has been involved
  - too numerous to mention individually

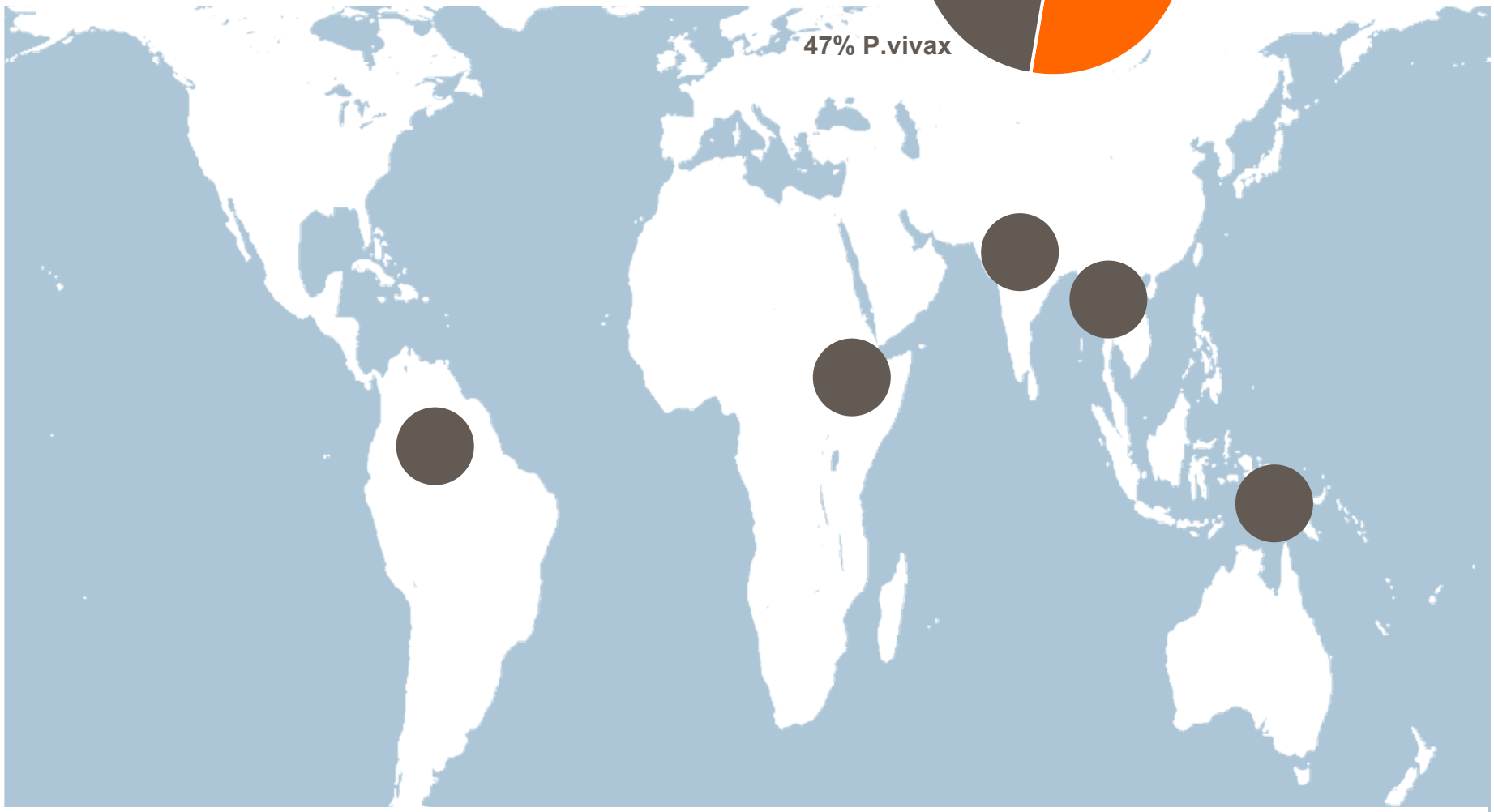
Disclosure

- I am an employee of GSK and hold stocks and shares in the company

Malaria Burden

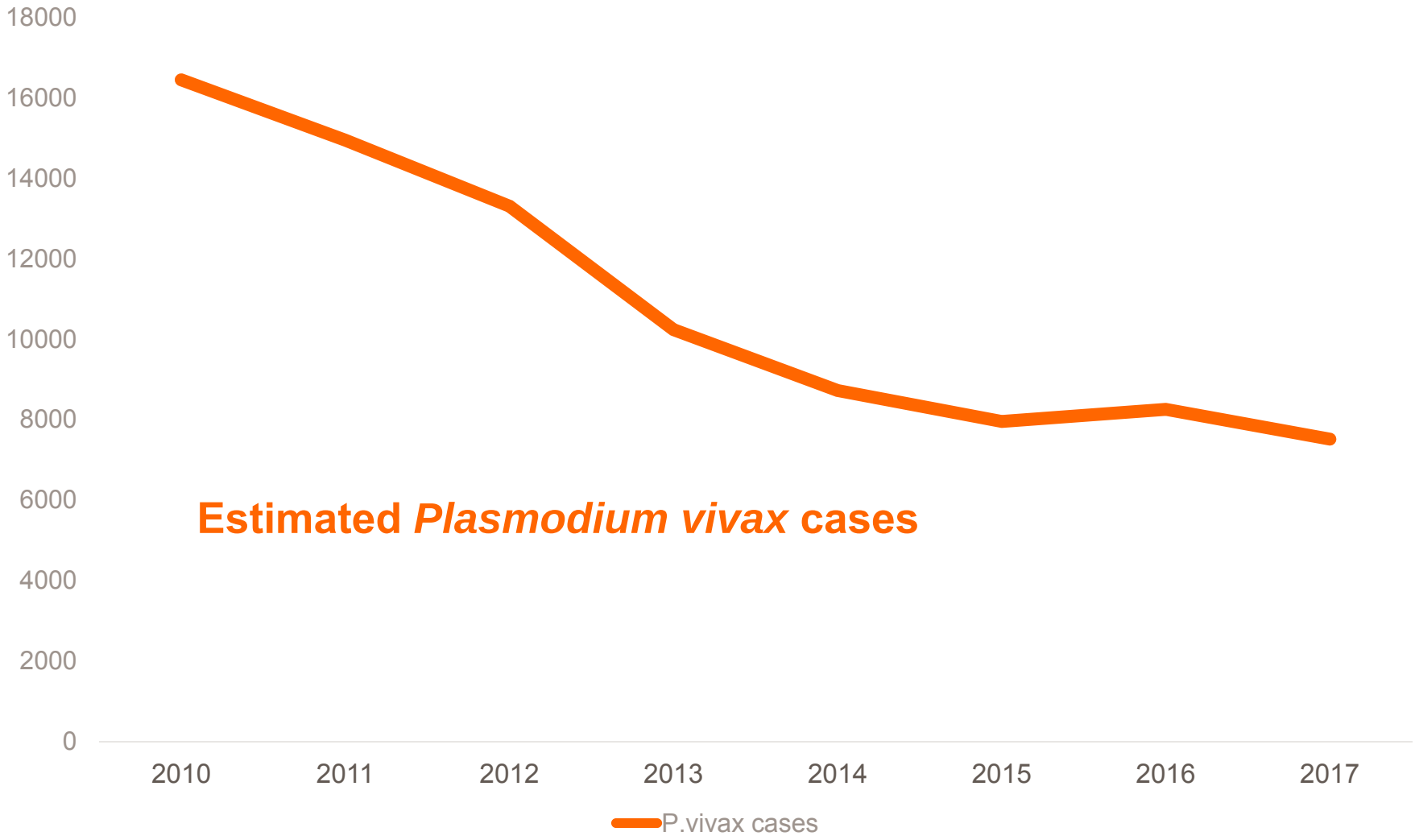
excluding sub-Saharan Africa





WHO technical brief on control & elimination of *P. vivax* malaria 2015

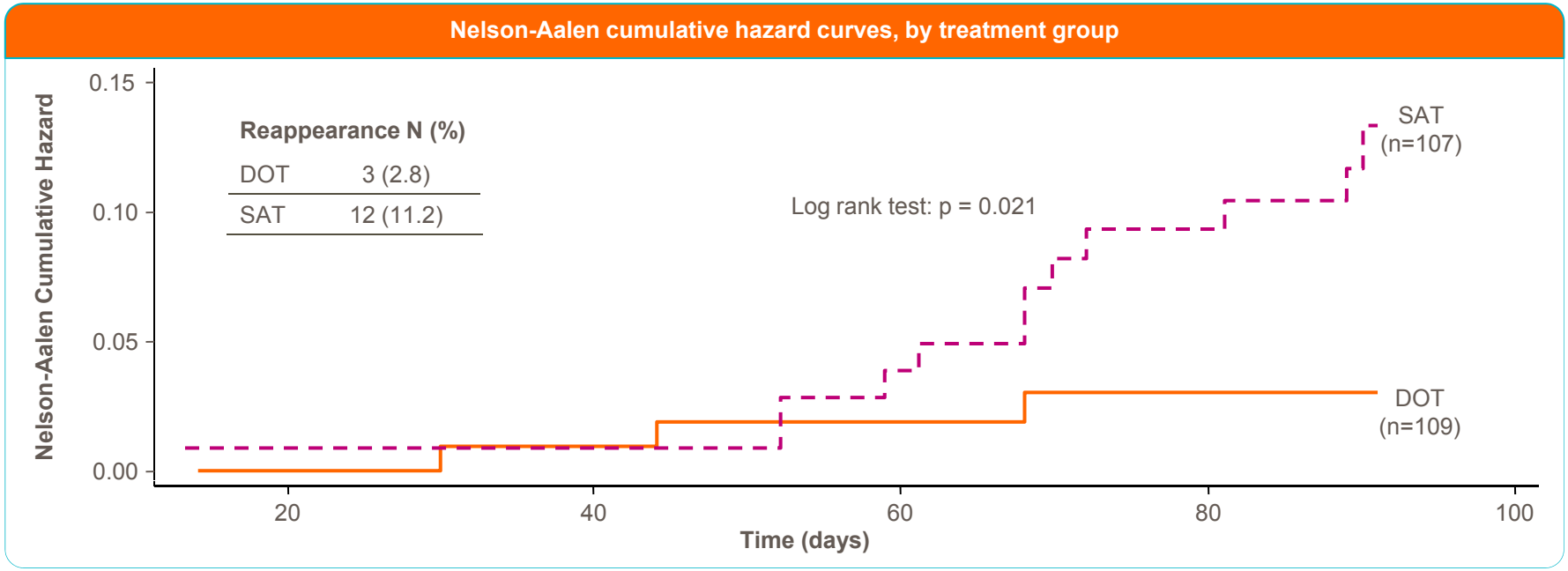
Progress towards elimination has slowed



WHO world malaria report malaria 2018

Adherence to PQ is a challenge and negatively affects risk of relapse

- To achieve a radical cure (cure and prevention of relapse) a 14 day course of primaquine is required
- For those that do receive the 14-day primaquine course there are significant problems with adherence to treatment

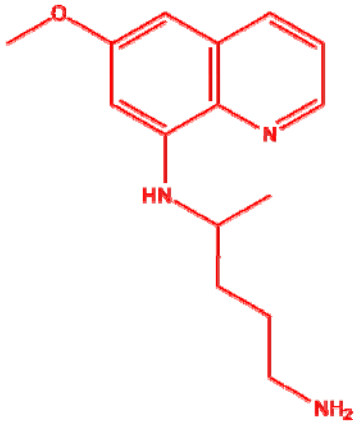


SAT: self administration therapy; DOT: directly observed therapy

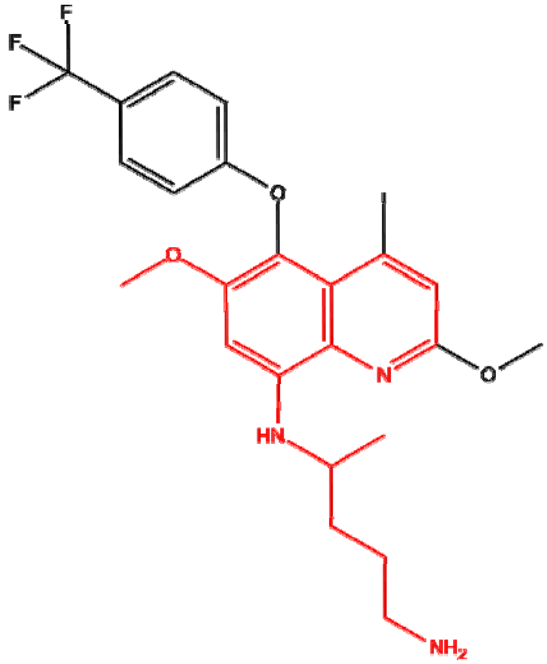
WHO technical brief on control & elimination of *P. vivax* malaria 2015
Takeuchi R et al. *Malaria Journal.* 2010; 9: 308

Tafenoquine molecular structure

- Long half-life in man (2–3 weeks)
- Single 300 mg dose

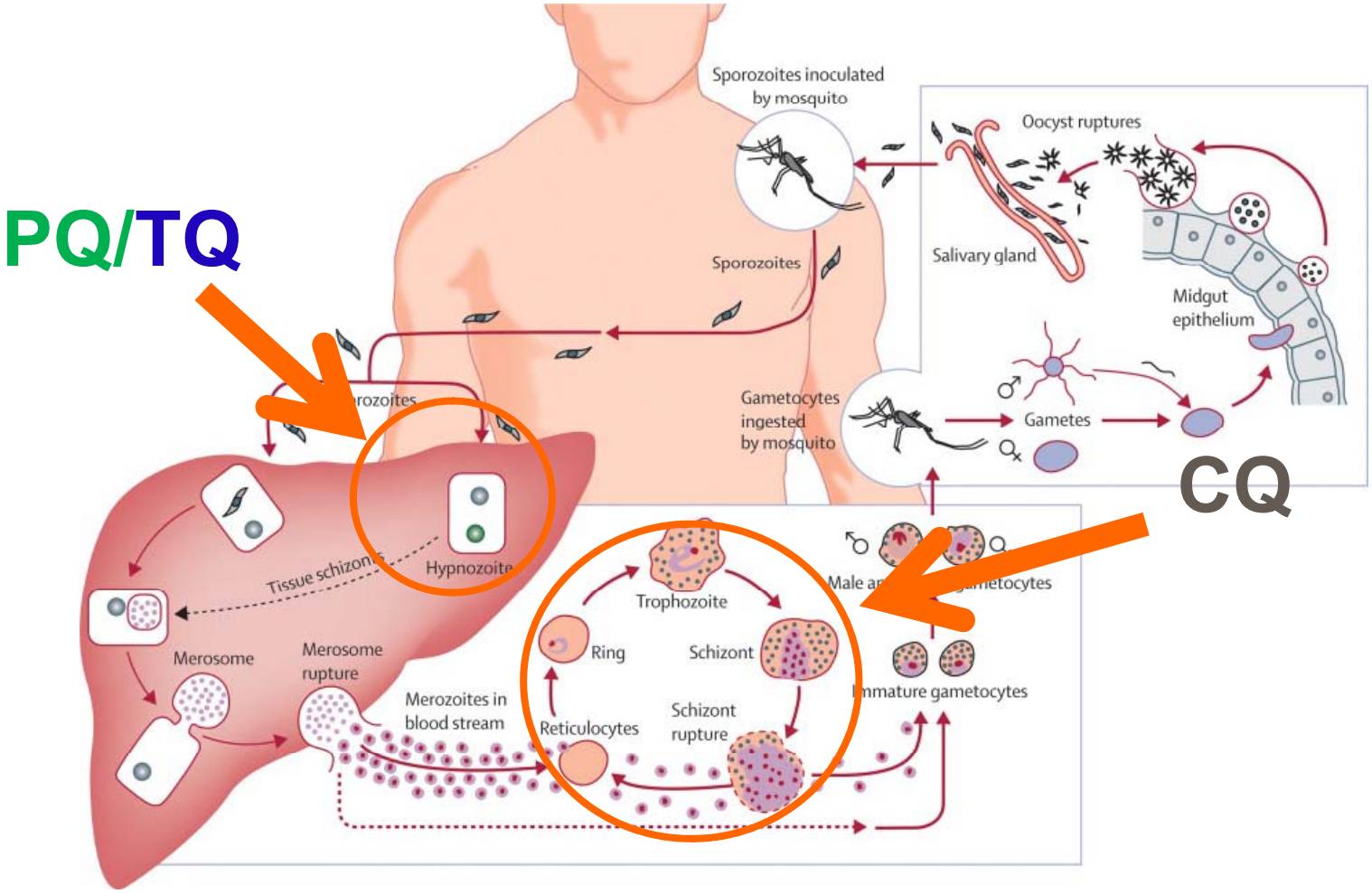


Primaquine



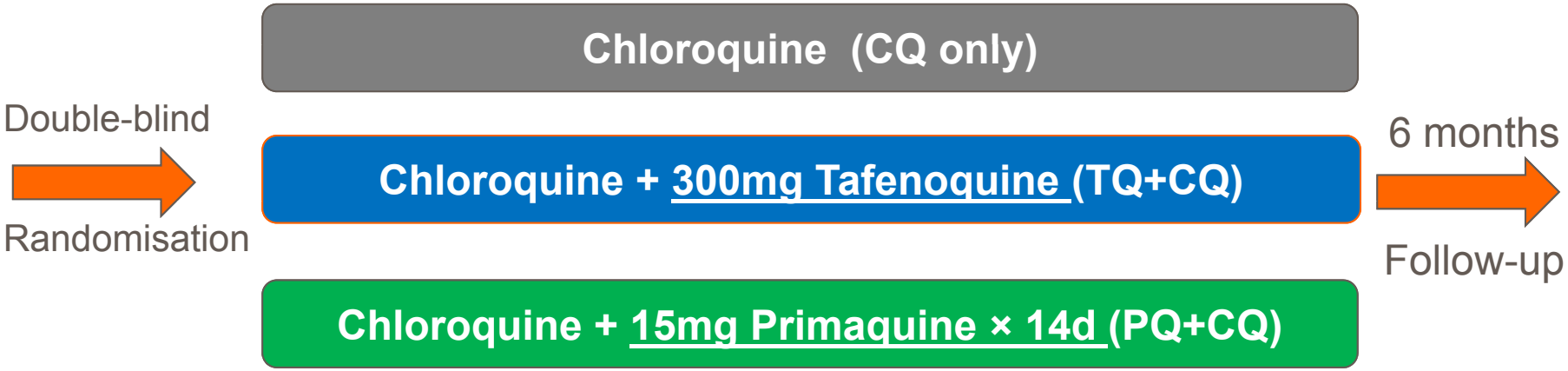
Tafenoquine

The primary TQ site of action is the liver



WHO technical brief on control & elimination of *P. vivax* malaria (2015)

DETECTIVE part 2: Multi-centre, double-blind, double-dummy, placebo-controlled



Randomisation ratio 1:2:1
Recruitment stopped early at 522/600 subjects following agreement with FDA

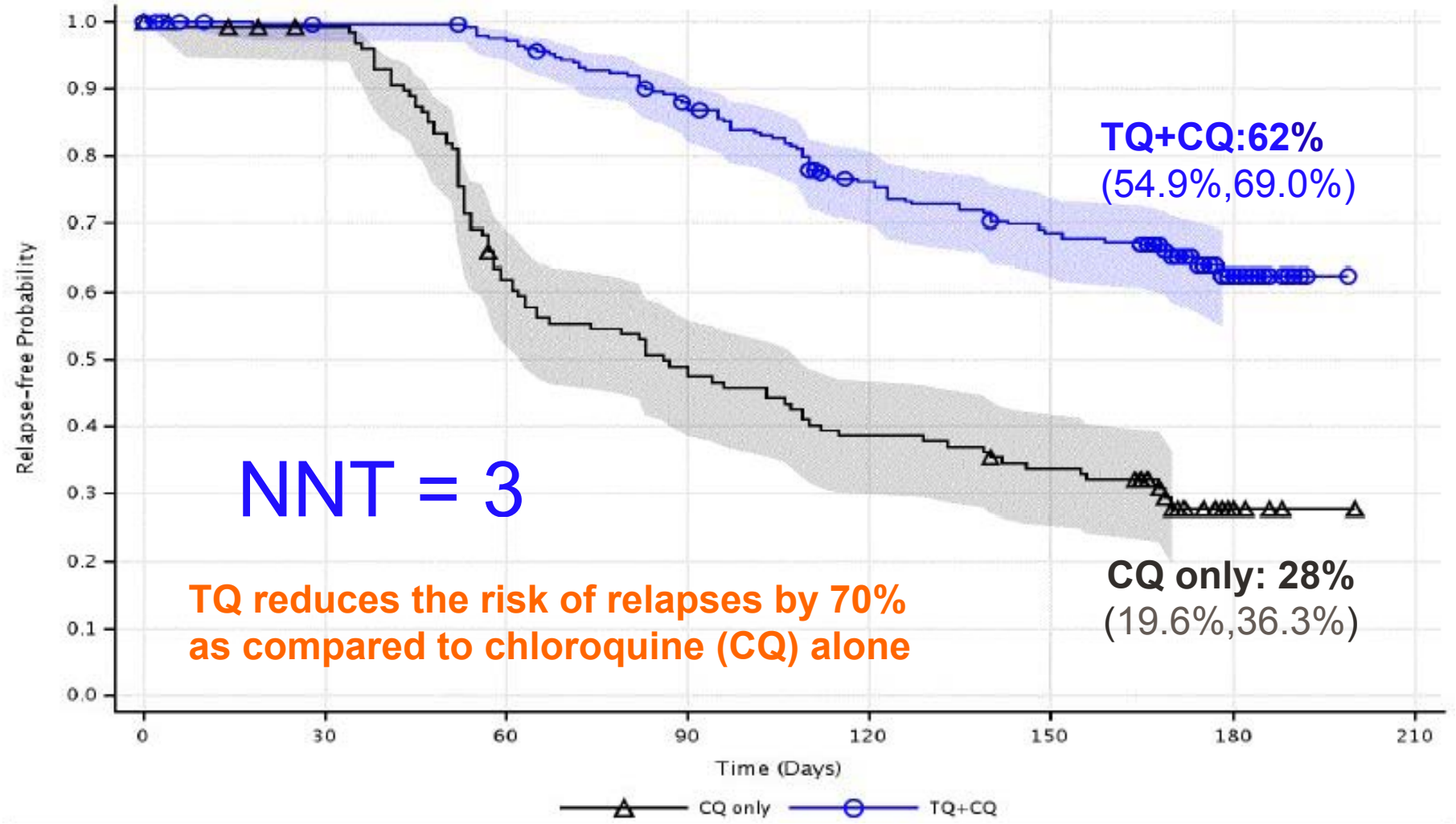
Key Inclusion Criteria

- Blood smear *P. vivax* **>100 – <100,000 parasites/µL**
- Age ≥16 years (Ethiopia ≥18 years)
- Females of non-childbearing potential or on contraception
- QTcF<450 msec

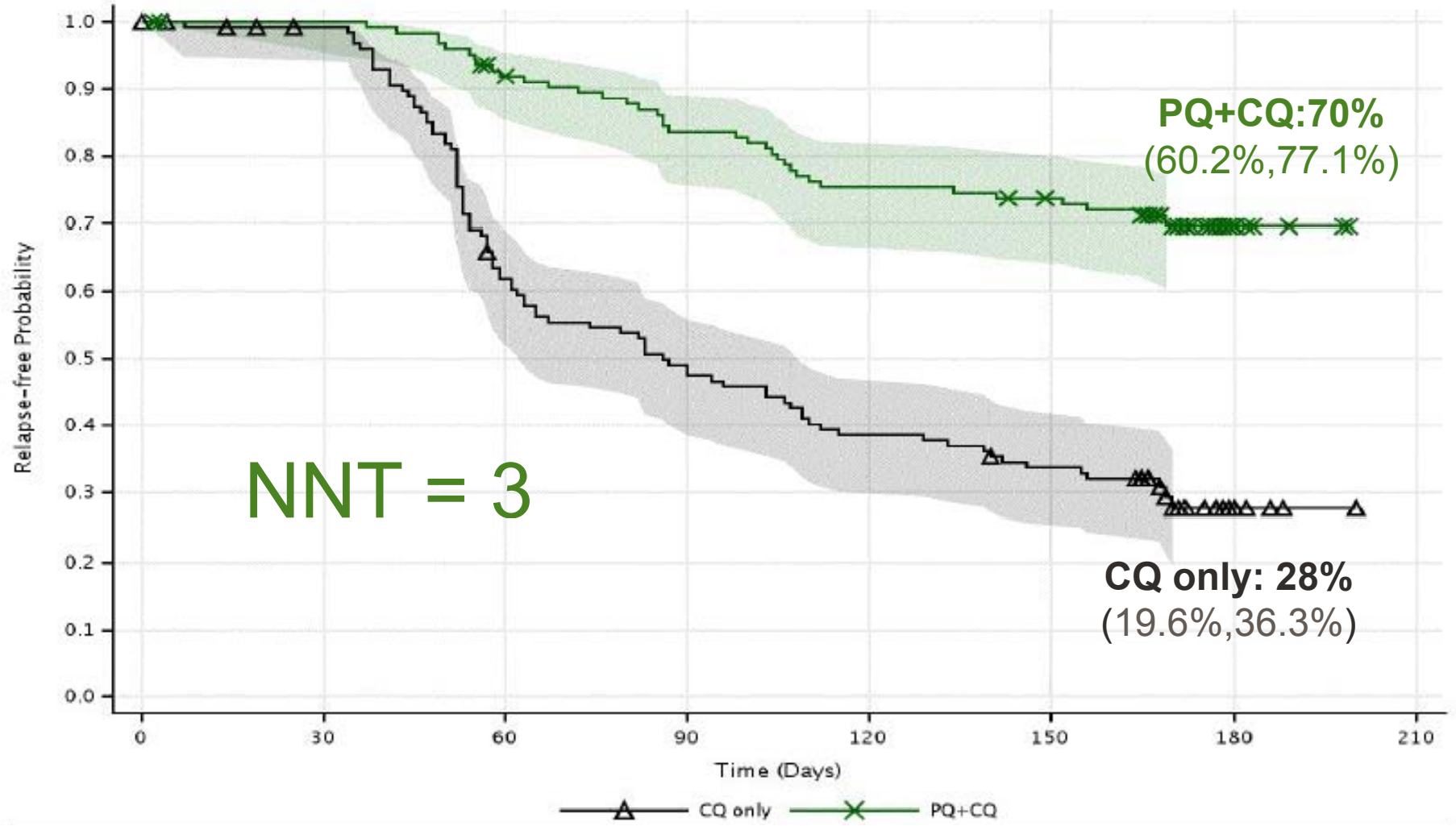
Key Exclusion Criteria

- **Mixed or severe *P. vivax* malaria**
- Severe vomiting
- Screening **haemoglobin <7 g/dL**
- **G6PD deficient (enzyme level <70% site median)**
- ALT >2×ULN
- Significant concurrent illness
- Anti-malarial treatment within past 30 days
- Allergy or contra-indication to study treatment
- Illicit drug abuse/alcohol excess

DETECTIVE part 2
Relapse-free efficacy 6 months (mITT)

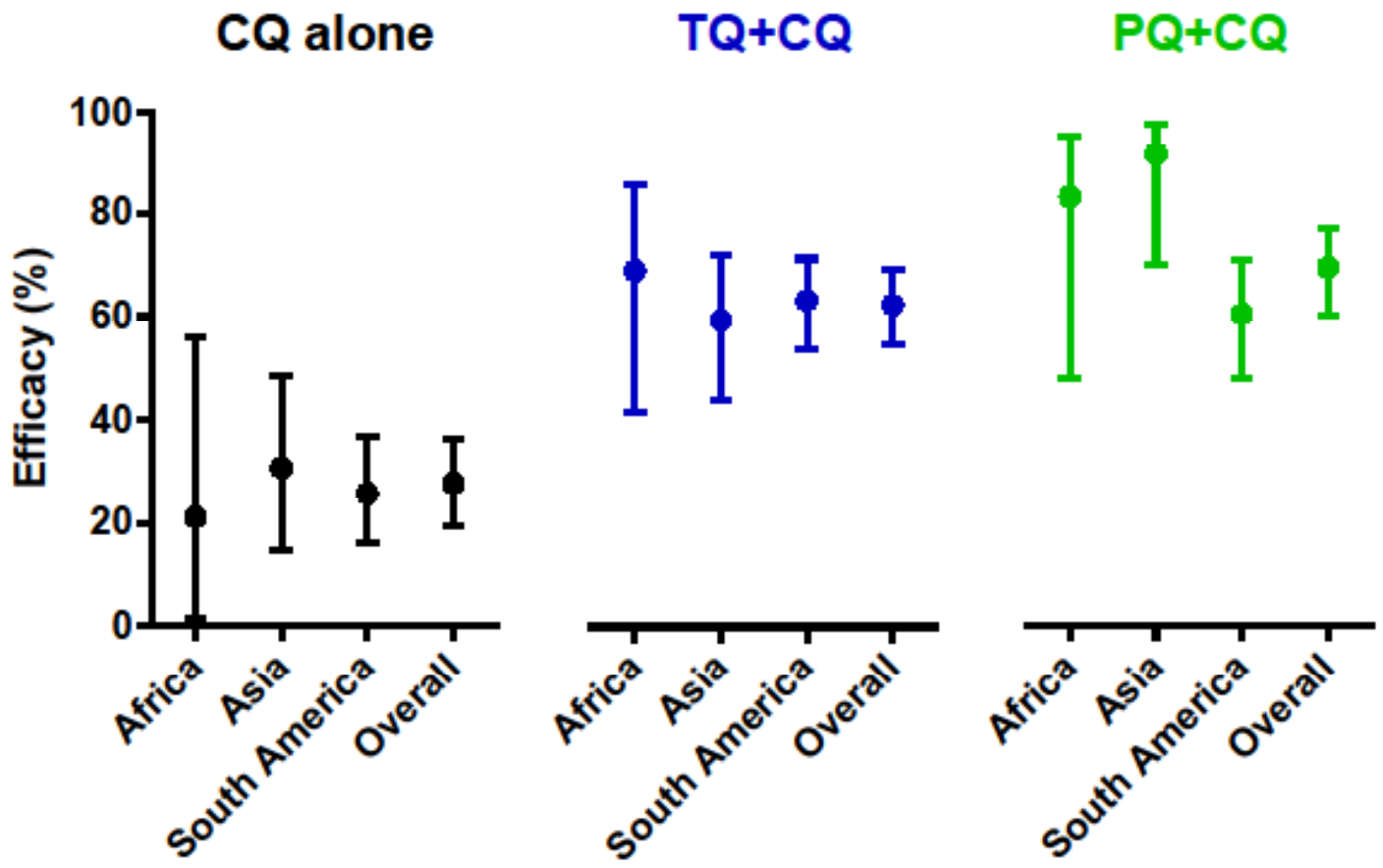


DETECTIVE part 2
Relapse-free efficacy 6 months (mITT)

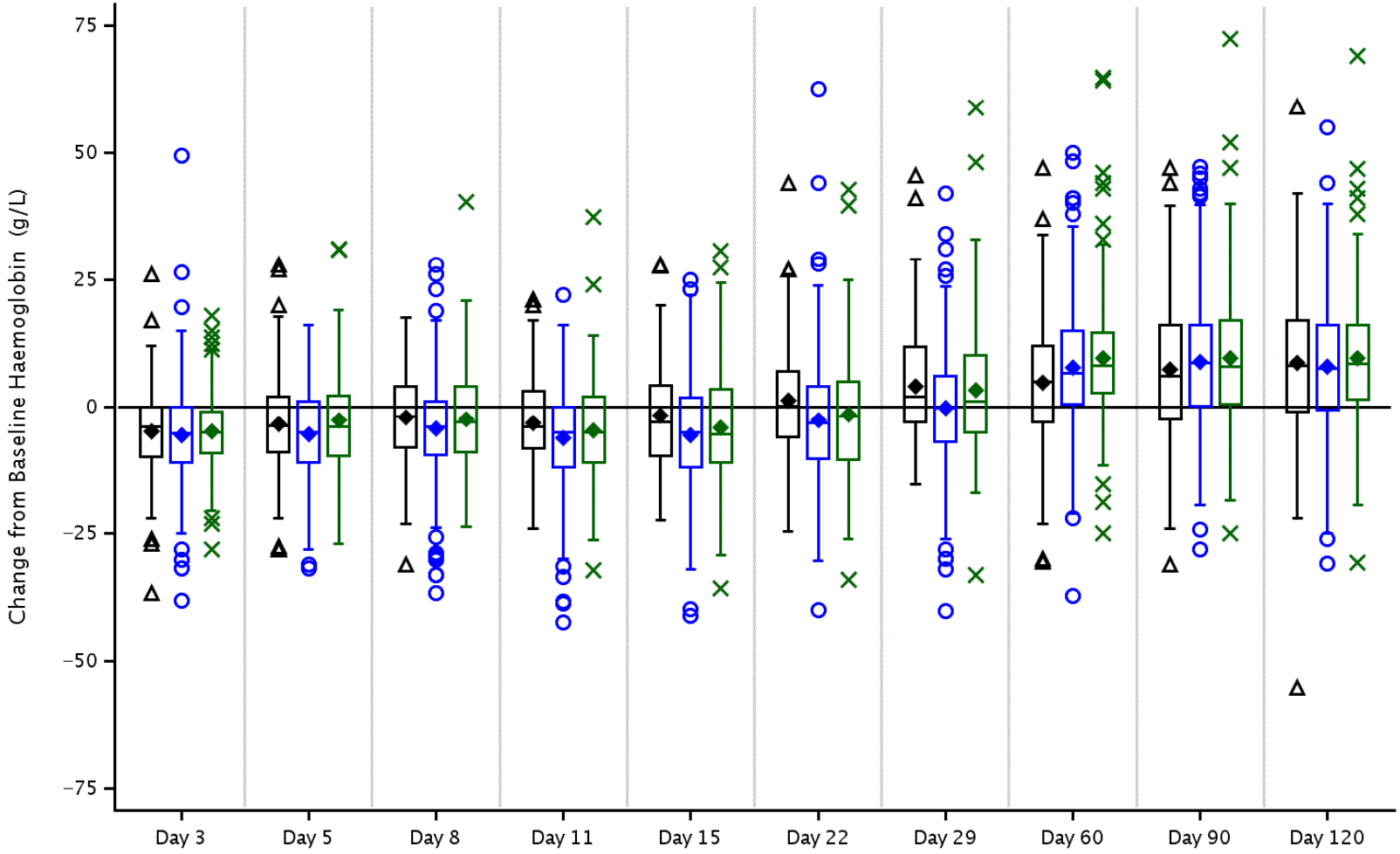


DETECTIVE part 2
Relapse-free efficacy 6 months by Region

Kaplan Meier Estimates and 95% CI by Treatment



DETECTIVE part 2 : Change from Baseline Hb balanced across treatment arms



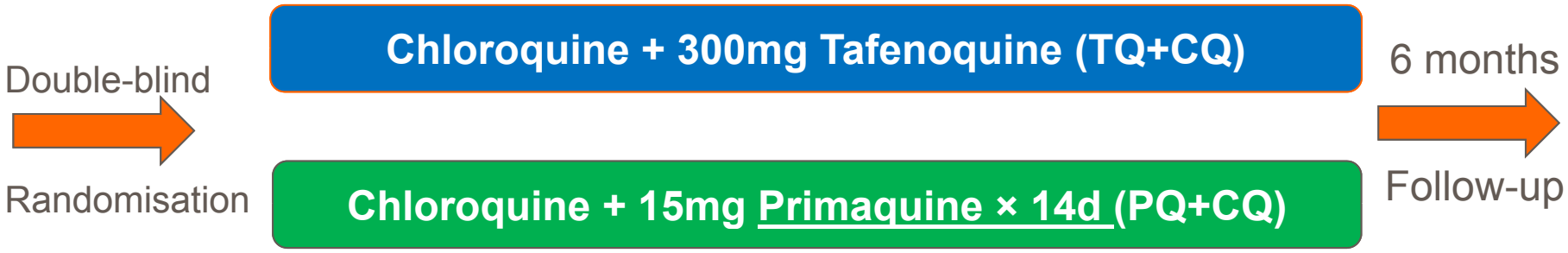
Chloroquine Tafenoquine Primaquine

GATHER Study Design

Total sample size planned was 300 subjects:

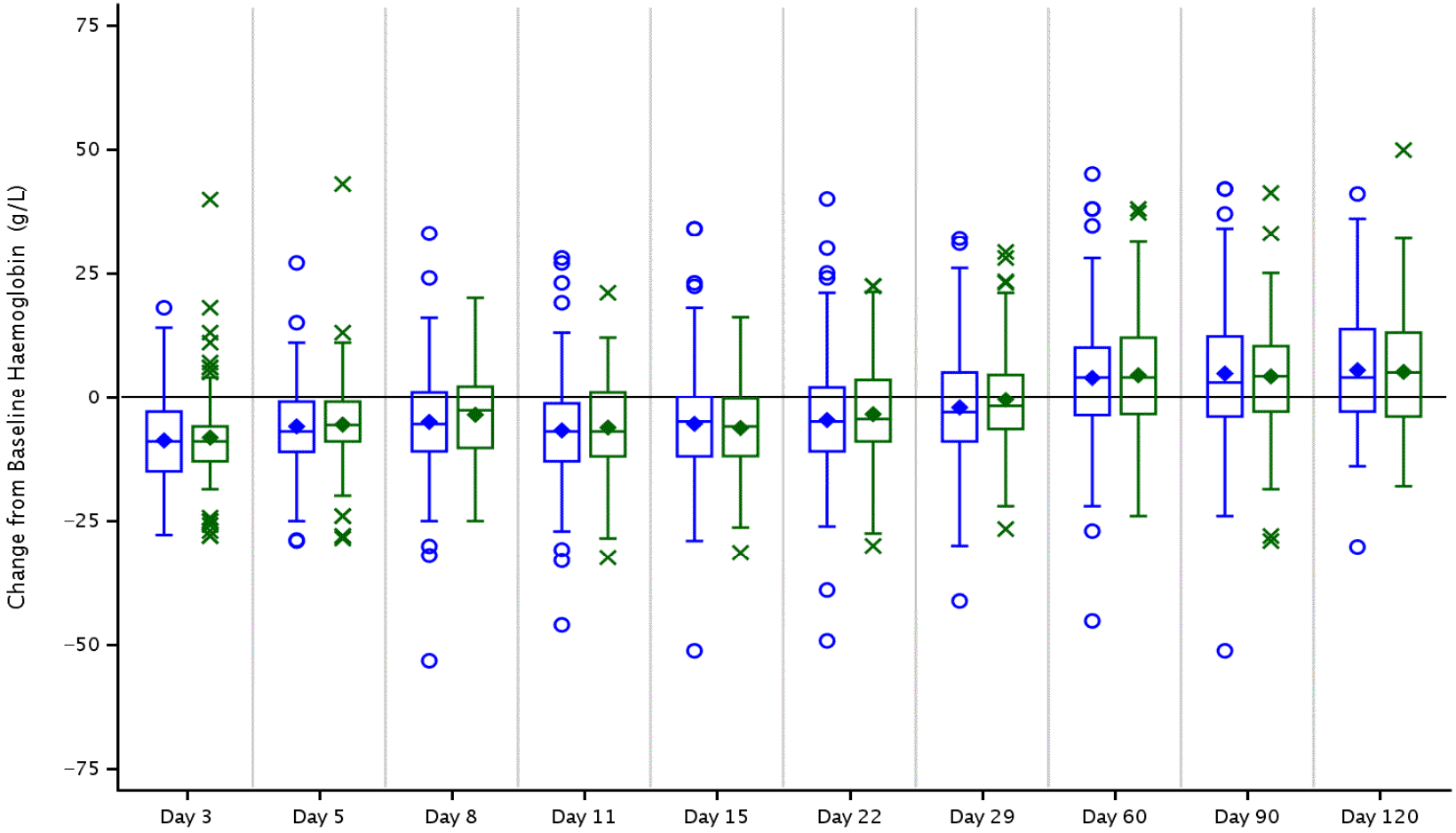
- **250 subjects (G6PD activity >70%)**
- 50 females (G6PD activity ≥40%-<70%)

Subjects randomised in ratio 2:1, stratified by G6PD activity



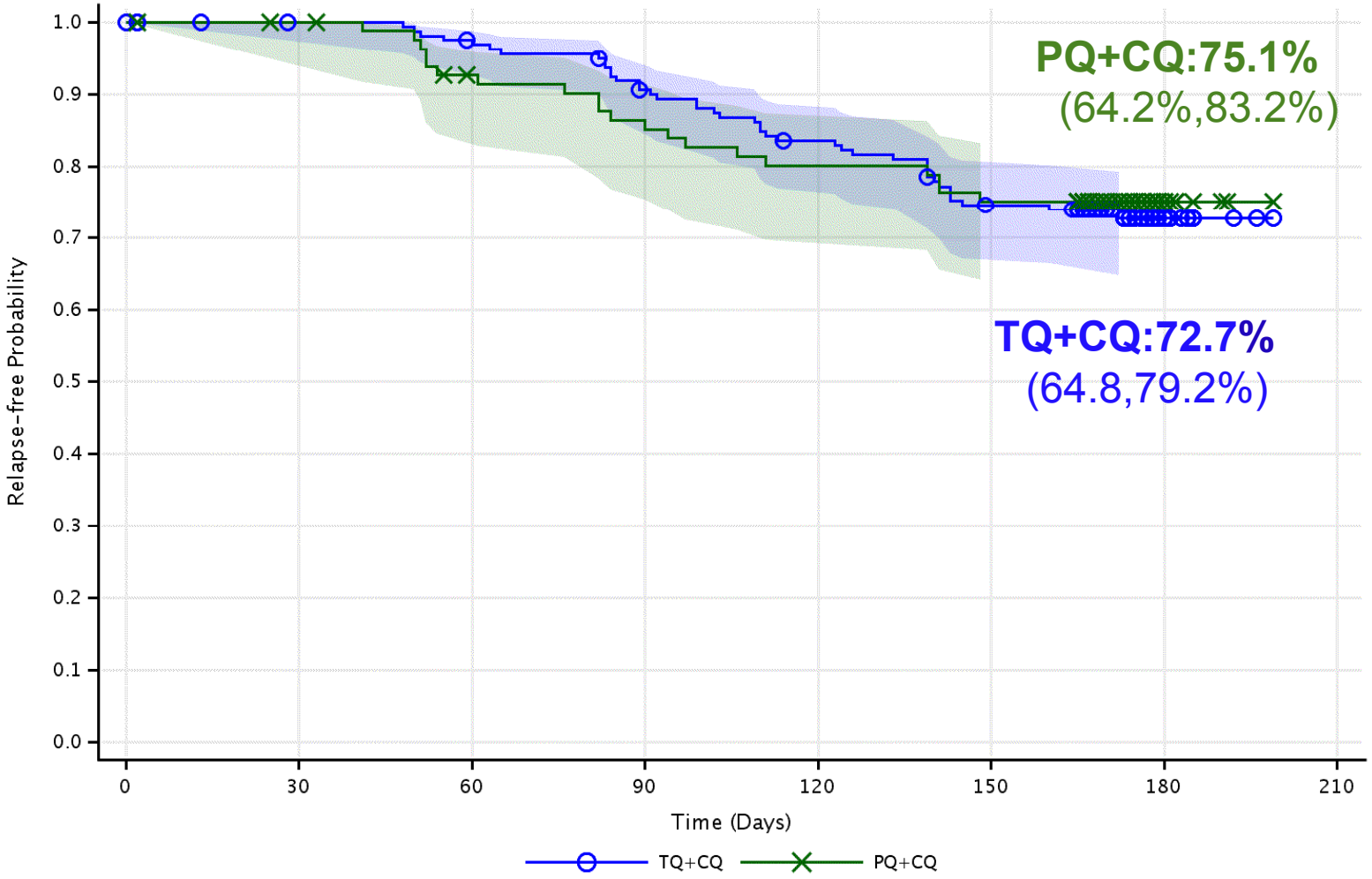
Note: Recruitment into moderate G6PD activity(≥40%-<70% of site median) continued for additional 6 months. 1/50 female G6PD moderate subject was enrolled.

GATHER Change from Baseline Hb - Consistent with DETECTIVE



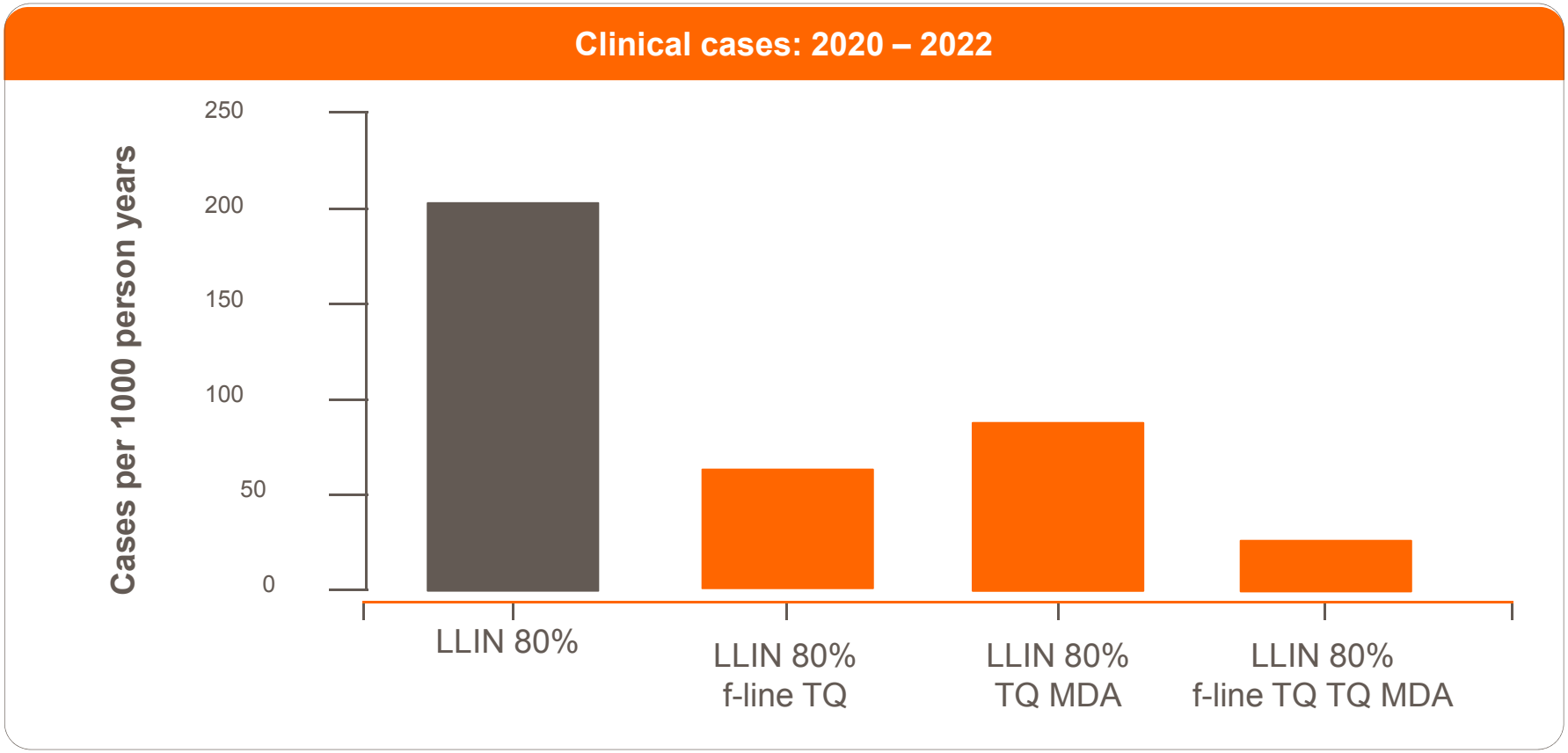
Tafenoquine Primaquine

GATHER
Relapse-free efficacy 6 months (mITT)



Large reductions in transmission could be achievable with access to tafenoquine

Model projections of *P. vivax* in high transmission setting province (New Ireland, PNG)



LLIN: Long-lasting insecticidal nets; f-line: front-line; MDA: Mass drug administration; PNG: Papua New Guinea; TQ: Tafenoquine

White MT et al. *Nature Communications* 2018; 9(1): 3300-3310

Location of Planned Feasibility Studies

Quantitative G6PD testing plus tafenoquine

Conclusions

- A single-dose treatment with the potential to improve patient compliance could positively impact *P. vivax* control and elimination efforts
- TQ reduces the risk of relapses by 70% as compared to chloroquine (CQ) alone
- Feasibility studies will help to inform potential adoption of TQ in other countries affected by *P. vivax* malaria

Any Questions?