



GHIT, Takeda and MMV collaboration: Advancing DSM265 from candidate selection to phase IIa

Tokyo, 8 Dec. 2017

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MMV

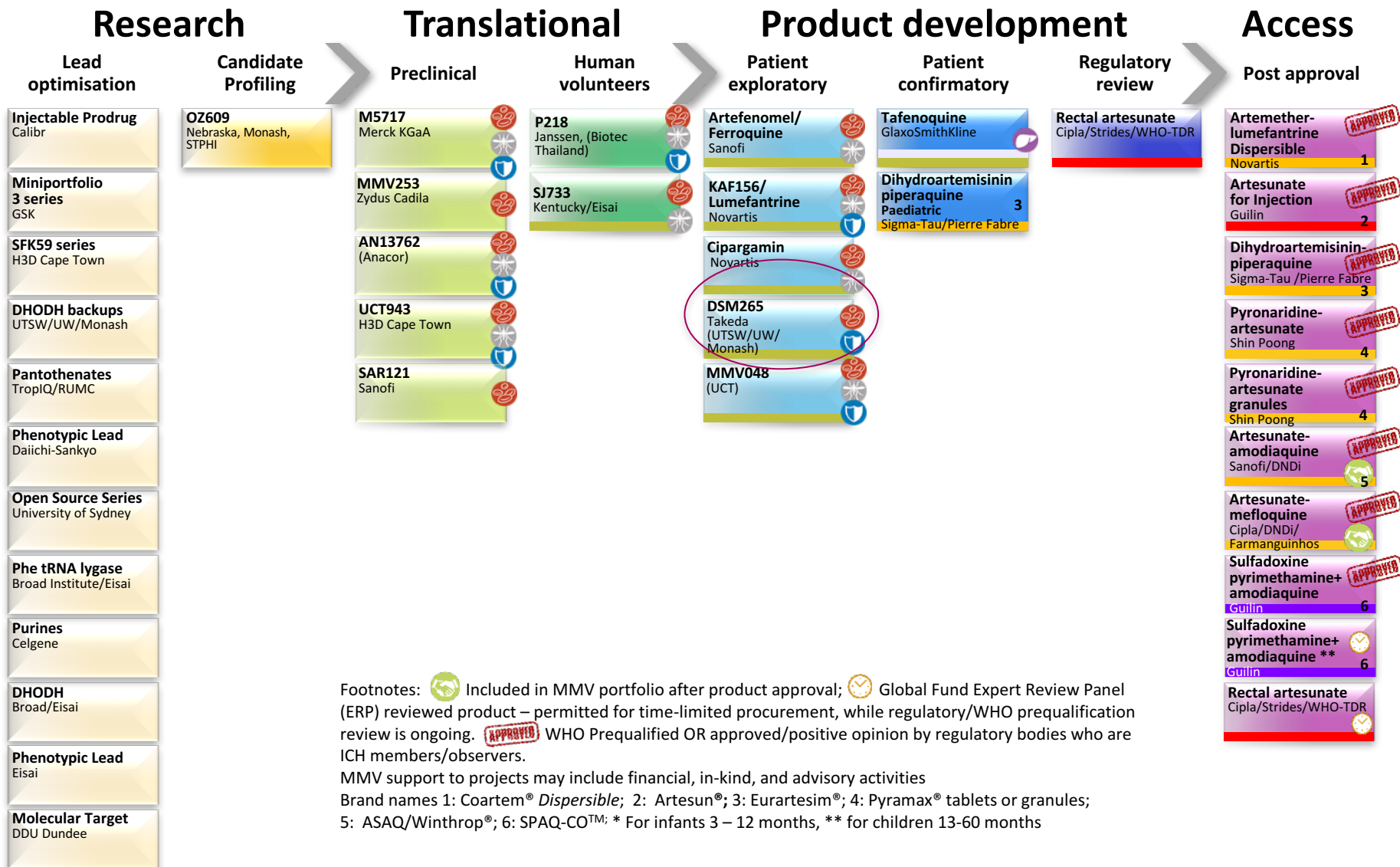
Defeating Malaria Together

MMV 
Medicines for Malaria Venture

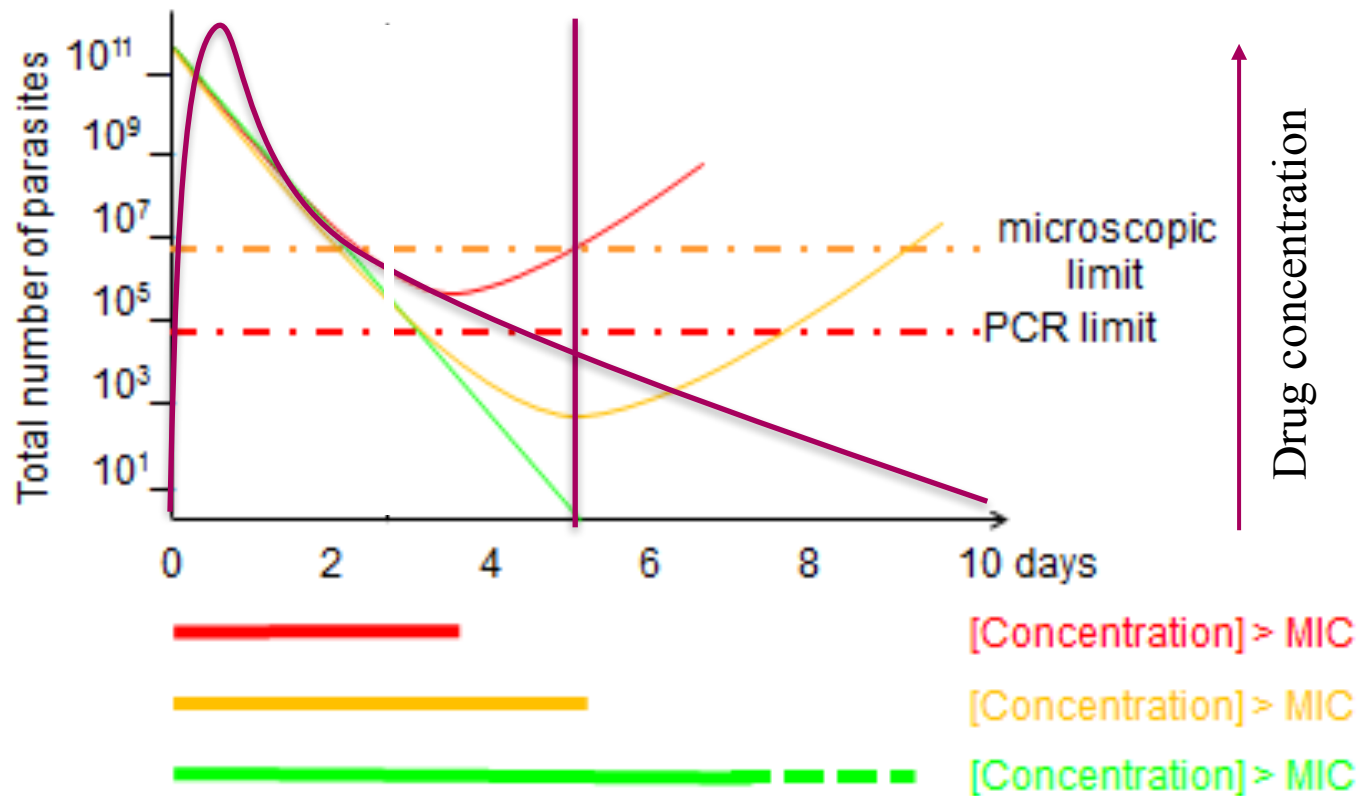
Agenda

- DSM265
- Determining early clinical activity
 - Asexual stage
 - Liver stage
- Identification of best combination

Strong pipeline of molecules in development

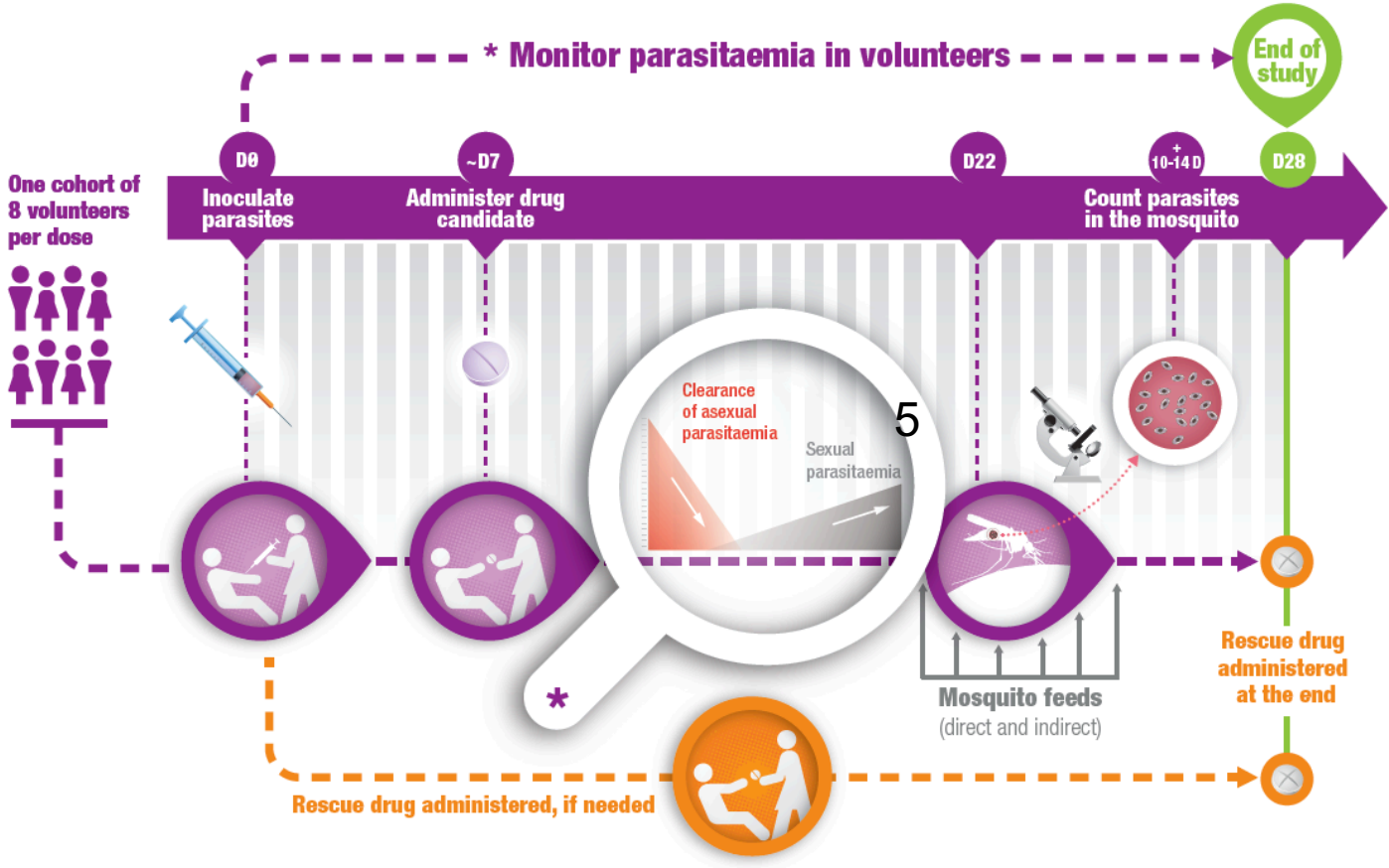


Determination of the Minimal Inhibitory Concentration



Nach NJ White (2013) *AAC*, 57, 5792

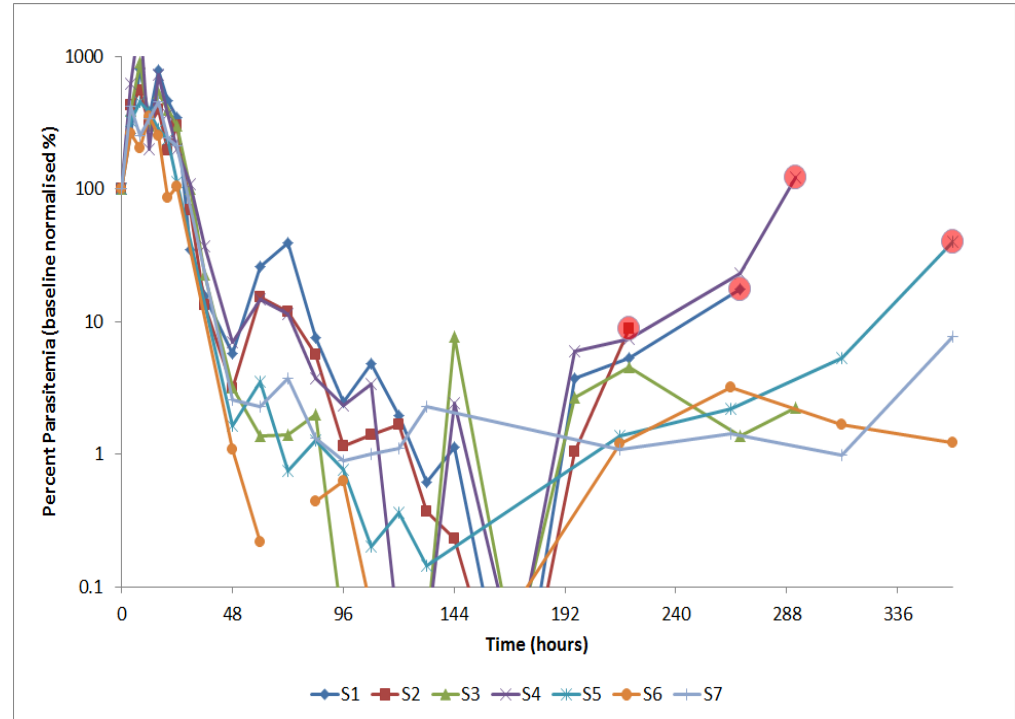
Blood Stage Challenge: TCP1, TCP5, TCP6



Challenge Studies to test NCE

DSM265 Phase I

- SAD
- 1 Challenge cohort (150 mg)
 - 3/7 cured
 - PRR approx 2
 - MIC 954 - 1400 ng/ml
 - HED~350 mg
 - 6 months after FiH



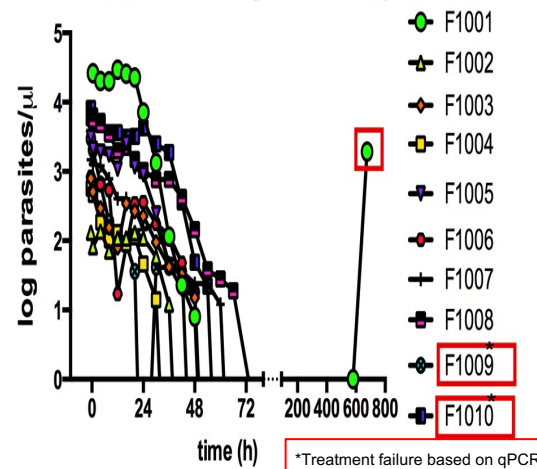
McCarthy et al. (2017) LID 17(6): 626

Can we transfer these results?

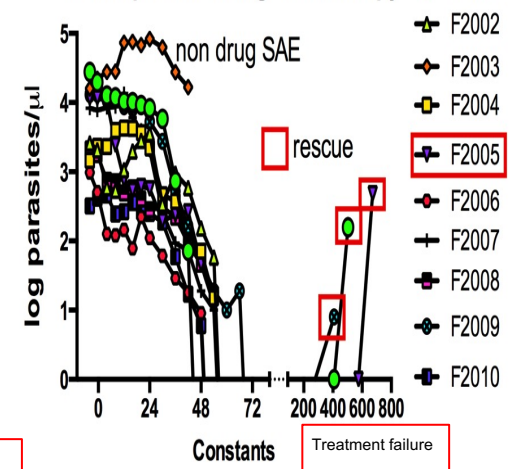
Phase IIa PoC Studie

- *P. falciparum*
2 cohorts (400, 250 mg)
- F/U period 28 days
- PRR, lag, MIC
- Study duration 7 m

P. falciparum 400 mg - Microscopy

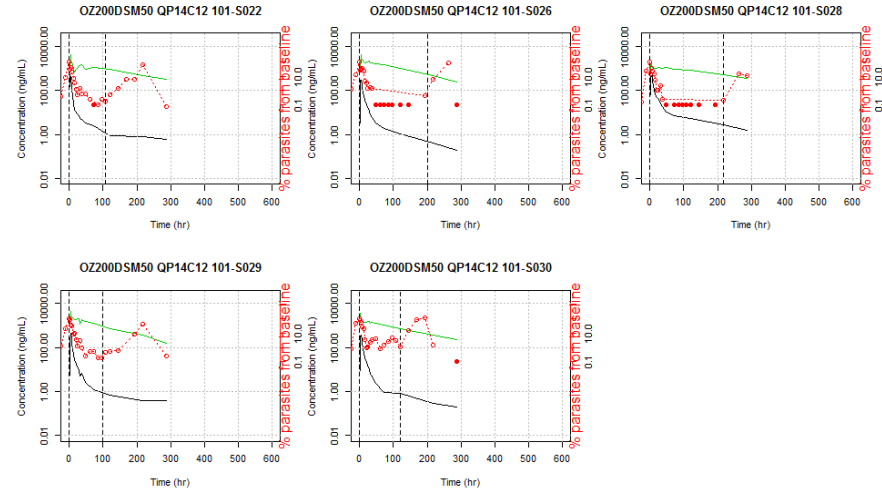


P. falciparum 250 mg - Microscopy



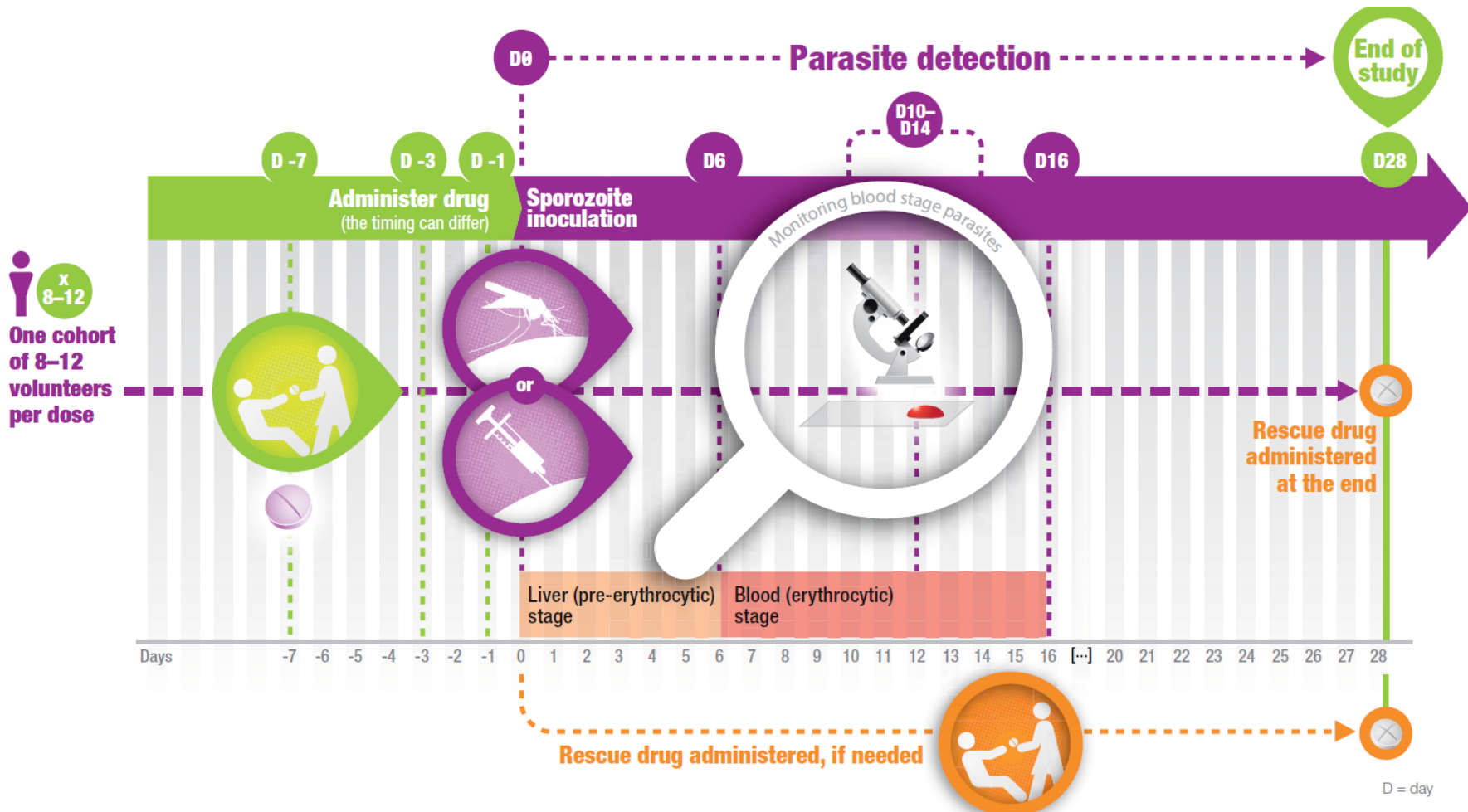
Pilot Combination Challenge Study

- Single dose of each drug that does not eliminate all parasites
- Low dose of OZ439 and DSM265 will allow observation of a combination effect
 - Change of PRR
 - Apparent MIC
 - Proportion of recrudescence
 - Time to recrudescence
 - Presence of gametocytes.
- 2 cohorts, 200/100 and 200/50 OZ439/DSM265
 - Cohort 1: 4/8 recrudescence
 - Cohort 2: 5/5 recrudescence



Drug	OZ439 200mg	DSM265 150 mg	OZ/DSM Combo 200 / 100 mg	OZ/DSM Combo 200 / 50 mg
Log ₁₀ PRR	2.2	1.5	2.8	2.7
95% CI	(2.1–2.3)	(1.4–1.7)	(2.6–3.0)	(2.6–2.8)
OZ439 MIC (ng/ml)	4.1		0.3	1.2
DSM265 MIC (ng/ml)		954–1400	573	709

CHMI model for chemoprotection/ chemoprevention activity TCP4

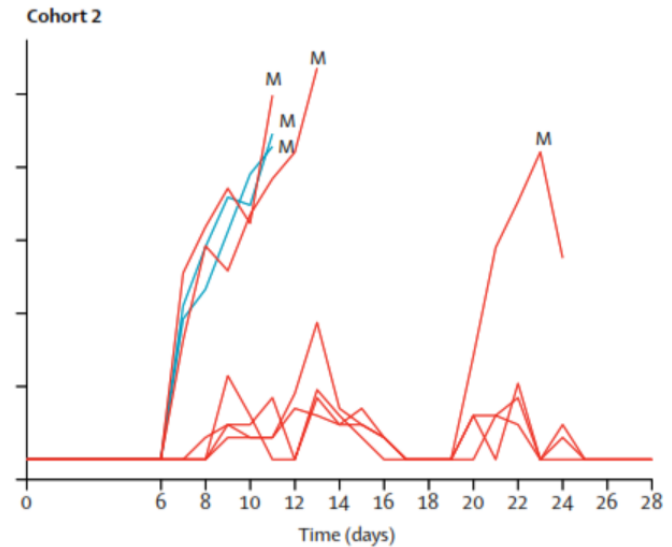
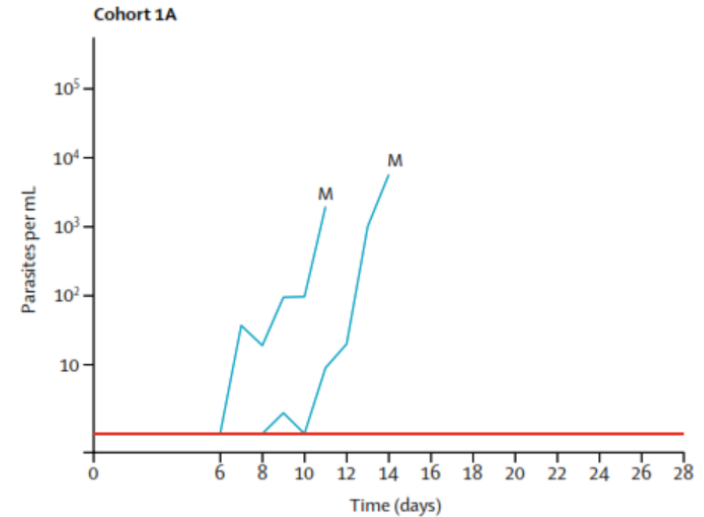


DSM265 Results

DSM265 protects when administered 1d before challenge

Breakthroughs when administered 7d before challenge

Once weekly could protect form infection due to combination of liver and blood stage activity



Sulyok et al. TLID March 2017

Our partnerships are our greatest strength



Global Health Innovative Technology Fund



Australian Government
AusAID

BILL & MELINDA
GATES foundation

ExxonMobil.



Irish Aid
Department of Foreign Affairs
An Roinn Gnóthaí Eachtracha

National Institutes of Health
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