

ASMQ FDC a simple and child friendly ACT developed for Asia and Latin America

ECTMIH

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FACT Project Manager

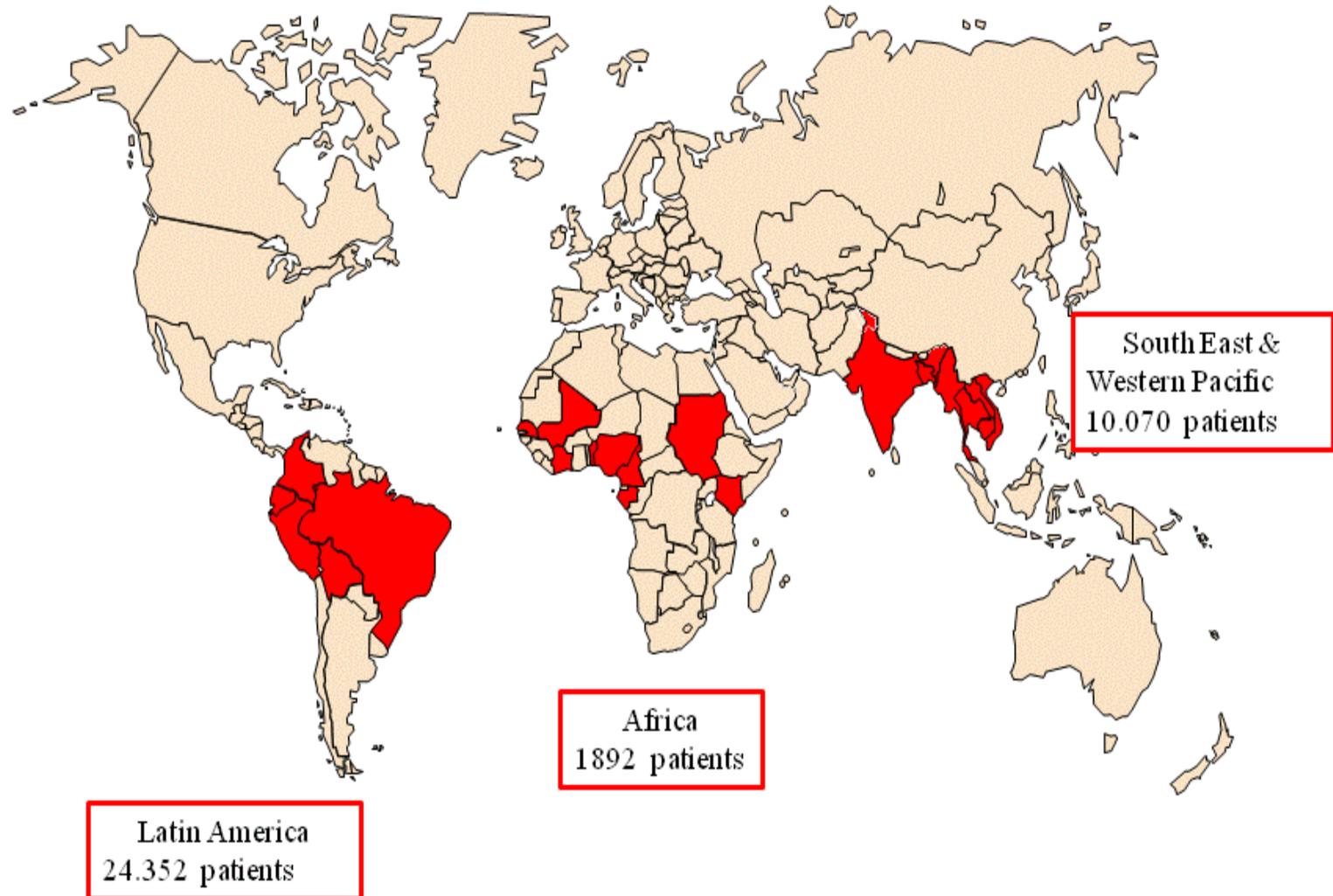
Drugs for Neglected Diseases *initiative (DNDi)*

DNDi

Drugs for Neglected Diseases *initiative*

Iniciativa Medicamentos para Enfermedades Olvidadas

**AS-MQ used over 19 years since 1992 in 3 continents,
Clinical data reported from more than 36.000 patients, 81
studies in 20 countries**



Artesunate-Mefloquine Fixed Dose Combination

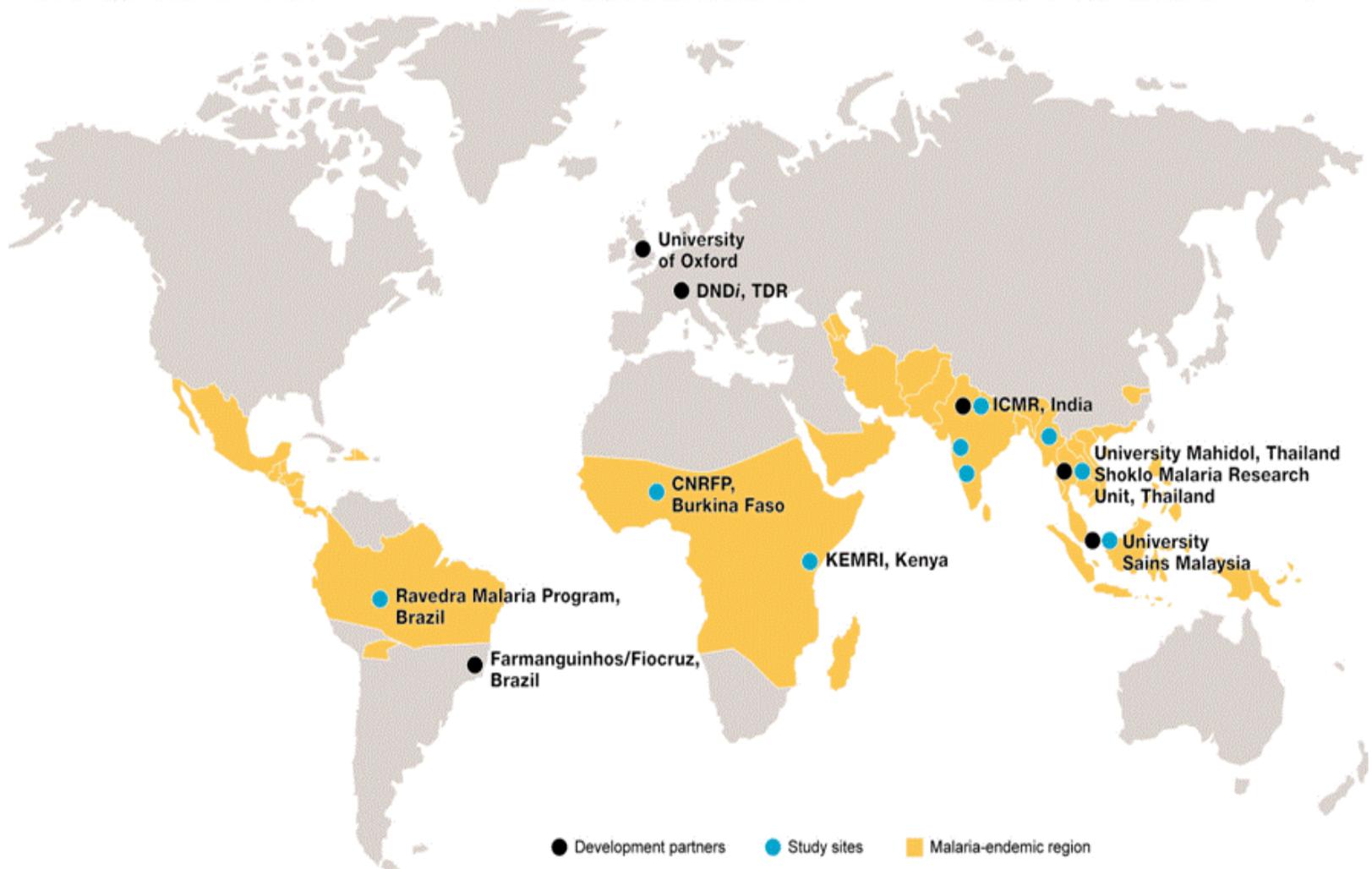
Industrial Partners:
Farmanguinhos
Cipla



FACT Development Team
DNDi/TDR:
scientific coordination
& project management



Funding: EU's INCODEV,
France, Netherlands,
Spain, UK, MSF

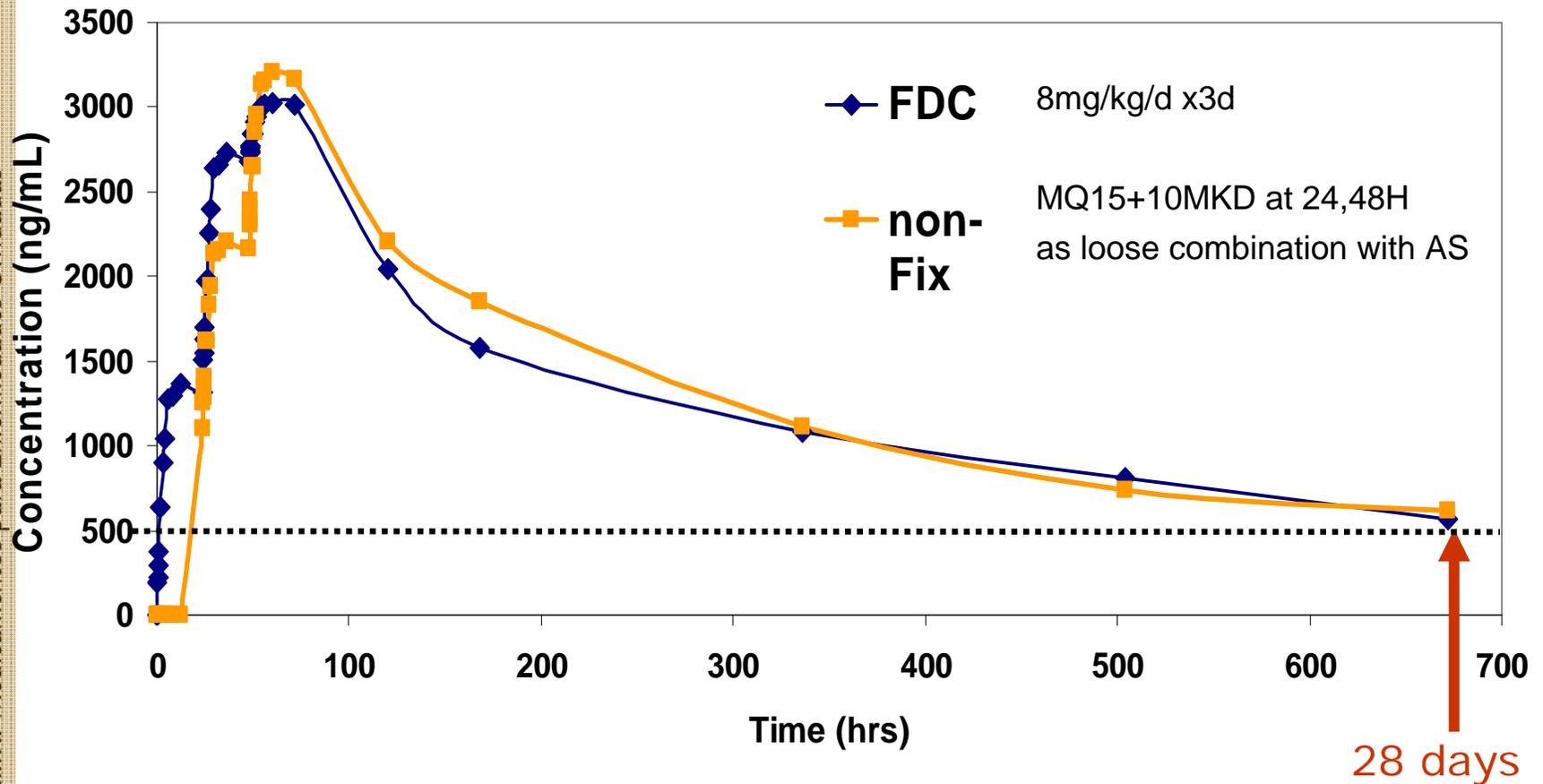


The Blueprint of ASMQ Tablet

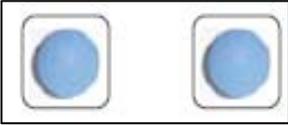


- Quality components (AS, MQ, excipients)
- Smallest possible size (Minimum excipients)
- Good aspect (Coating)
- Paediatric strengths; rapid disintegration in water
- Simple (1 or 2 tablets for 3 days)
- Stable (Process and Tropical conditions)
- Adequate biopharmaceutical properties

Predicted and Measured Profiles for MQ in Adult Patients (Thailand)



ASMQ FDC: pragmatic dosing regimen

Recommended Dosage for ASMQ FDC Tablets				
Asia		Latin America		Recommended Dose, daily for 3 days
Weight (Kg)	Age	Weight (Kg)	Age	
5 – 8	6 -11 months	5 – 8	6 – 11 months	 ASMQ FDC Tablet 25/55 mg ¹
9 – 17	1 – 6 years	9 – 17	1 – 5 years	 ASMQ FDC Tablets 25/55 mg ¹
18 – 29	7 – 12 years	18 – 29	6 – 11 years	 ASMQ FDC Tablet 100/220 mg ²
≥ 30	≥ 13 years	≥ 30	≥ 12 years	 ASMQ FDC Tablets 100/220 mg ²

¹Mefloquine HCl 55 mg are equivalent to 50 mg of mefloquine

²Mefloquine HCl 220 mg are equivalent to 200 mg of mefloquine

ASMQ

Small Tablets-Paediatric Strengths & Easy to use

ASMQ FDC
is easy to use
as 1 2 3!

1 dose 2 products 3 days

One single daily dose of 1 or 2 tablets of two highly effective combined products for three days of affordable medicine



INFANT
DOSE
< 1 YEAR

New FACT
ASMQ

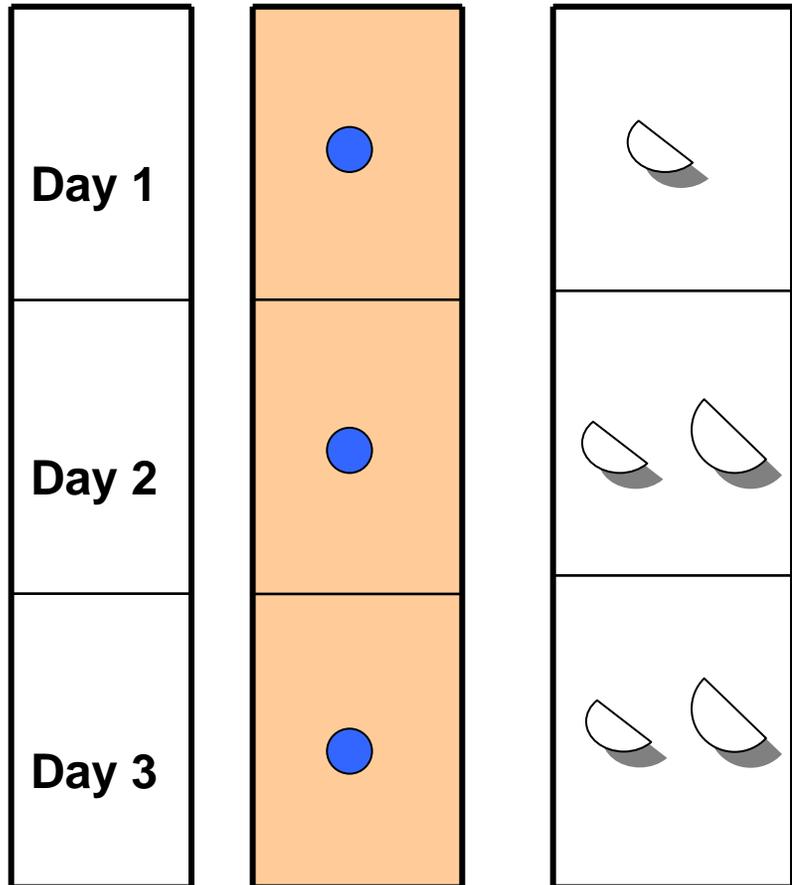
AS: 100mg
MQ(salt): 220mg

Once a day

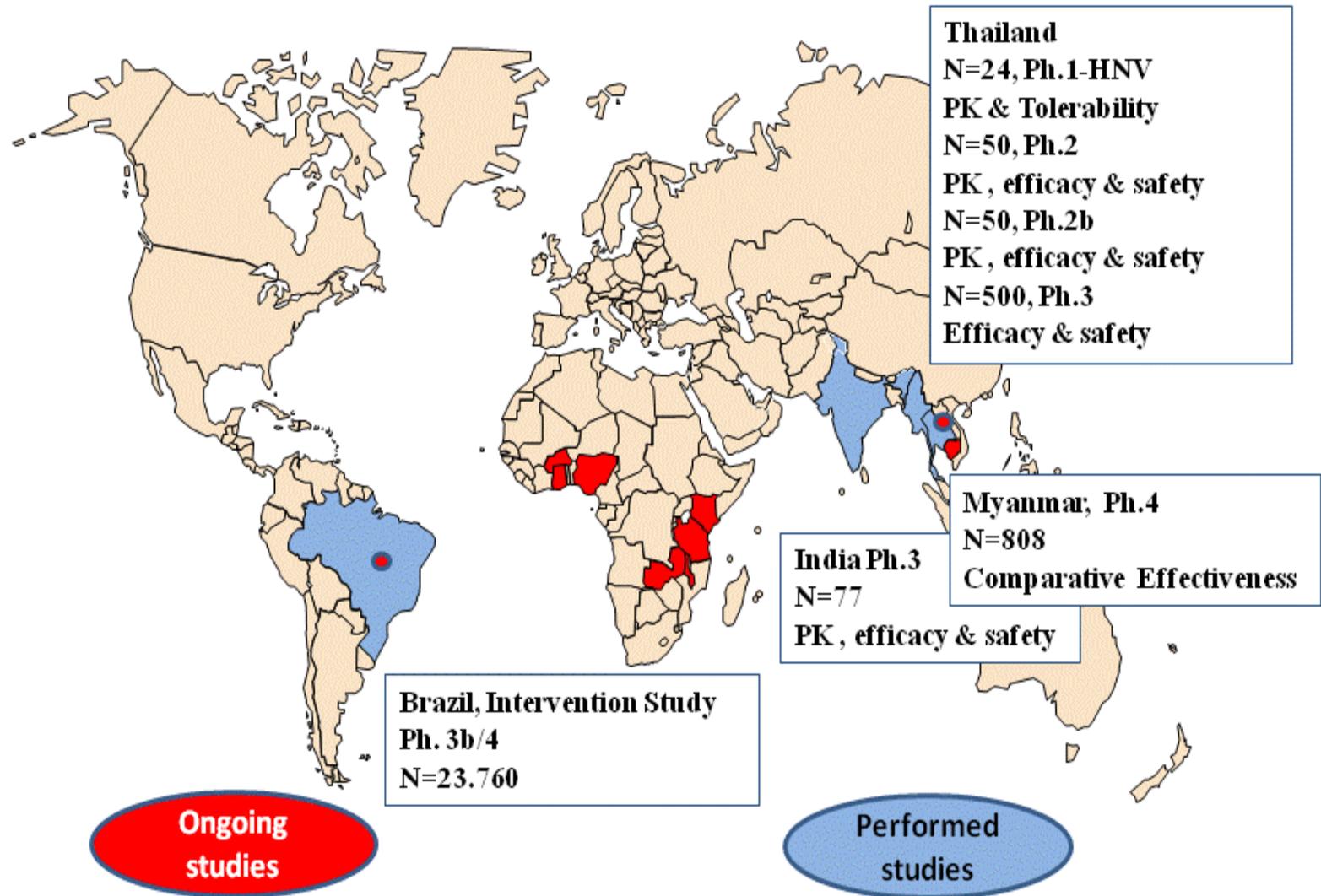
NON-FIXED
AS and MQ

AS: 50mg
MQ(salt): 250mg

Once a day



ASMQ FDC, Key studies performed and ongoing



ASMQ in Brazil

- **Phase IIIb/IV, intervention study** to evaluate the impact of programmatic use of ASMQ FDC in Acre and Pará (Amazon Basin) in comparison with standard regimen used in Brazil (MOH/PAHO/RAVREDA)
- **23.760 patients (including 8.880 children)** treated between 2006 and 2008

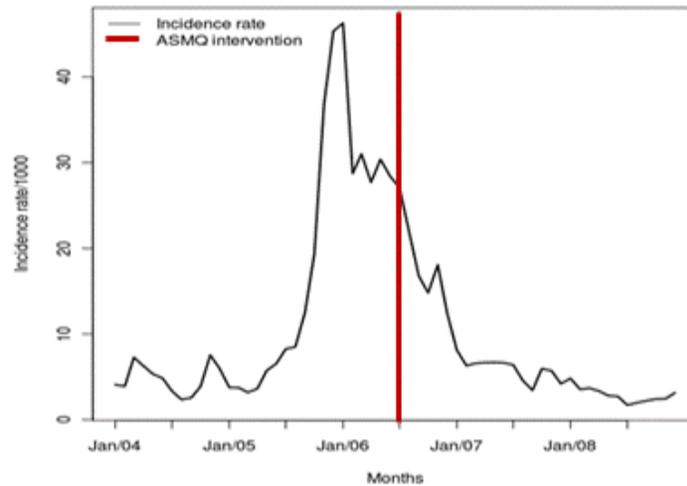
Safety

- ✓ No malaria deaths reported during the study period
- ✓ No serious adverse events reported
- ✓ No direct reports to the free-toll PV number from Farmanguinhos
- ✓ No reports to the national regulatory agency, ANVISA

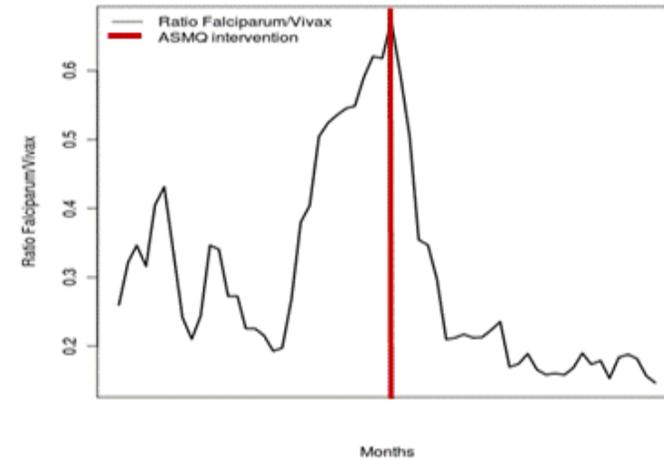


Effect of the artesunate mefloquine fixed dose combination in the malaria transmission in Amazon basin communities

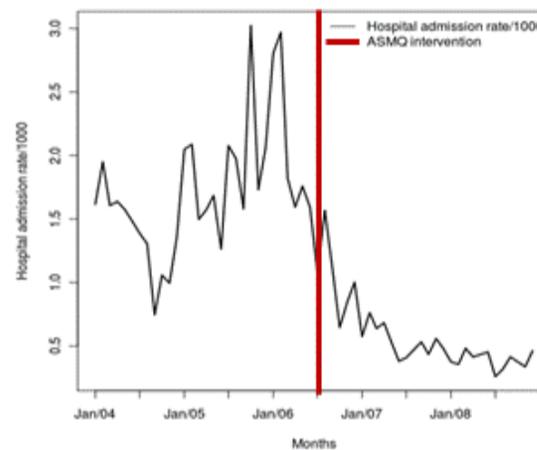
Incidence rate of malaria



Ratio *P. falciparum*/*P. vivax*



Hospital admissions due to malaria

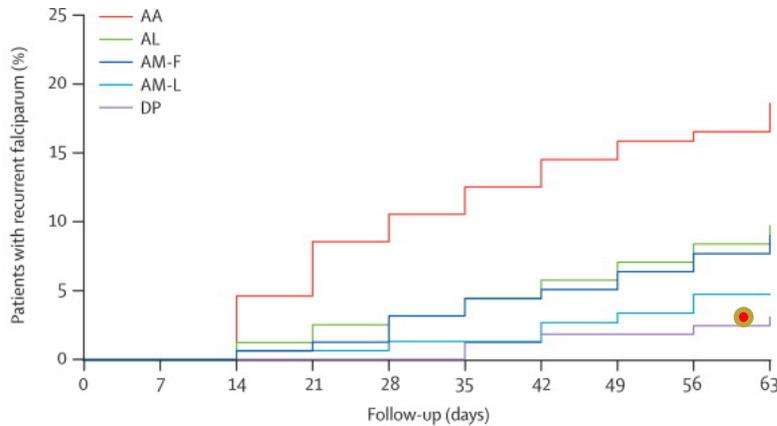


ASMQ FDC in Amazon Basin, subset analysis

Proportion of slides with asexual falciparum parasitaemia until D40 post-ASMQ treatment in Cruzeiro do Sul, stratified by age

Total patients	< 1 year	1 - 6 years	7 -13 years
3/584 (0.5%)	0/6 (0)	1/267 (0.37%)	2/311 (0.64%)

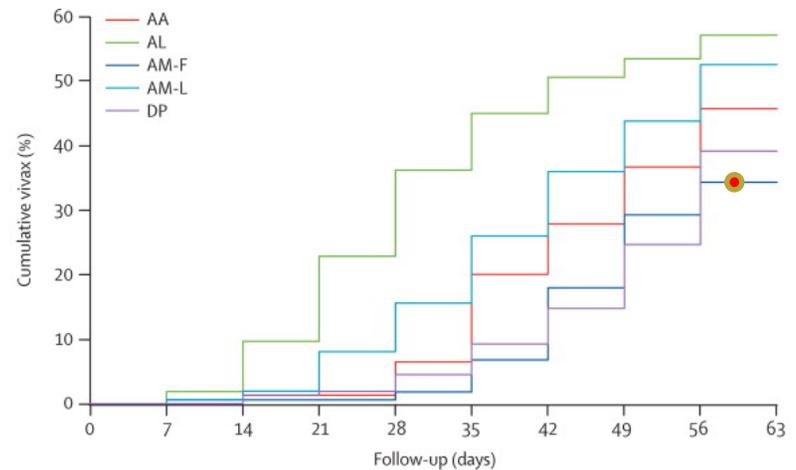
Comparing the effectiveness of 5 artemisinin combination treatment regimen in Myanmar



Number at risk

AA	155	155	152	145	138	135	132	128	124	122
AL	162	162	161	154	151	149	147	145	141	139
AM-F	169	169	165	165	165	164	161	160	159	157
AM-L	159	159	155	151	148	146	145	141	140	137
DP	160	160	159	158	156	152	148	146	143	140

Cumulative proportion of patients with vivax malaria during follow-up

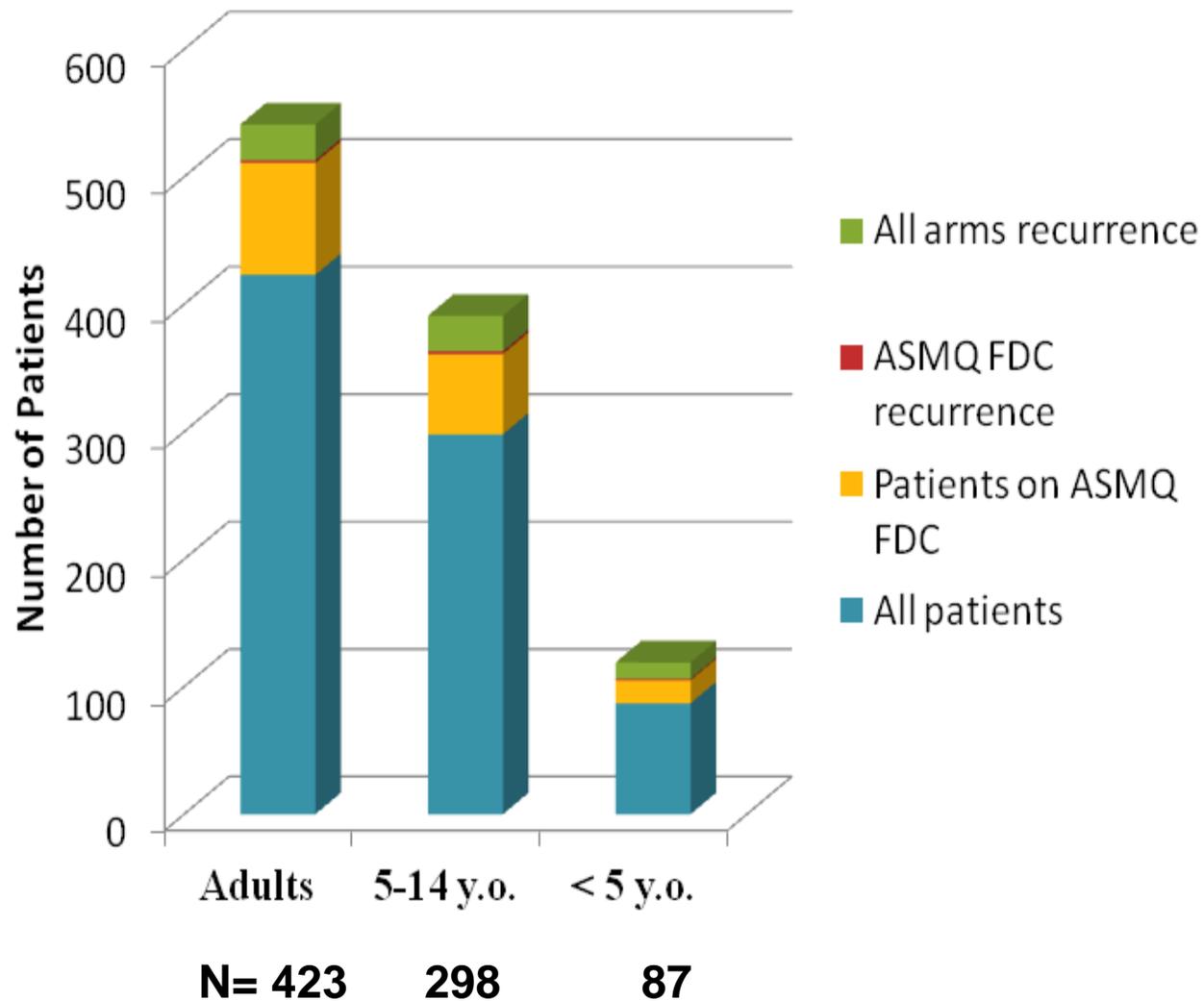


Number at risk

AA	155	155	152	144	137	134	124	103	90	77
AL	162	162	161	151	137	116	94	79	69	64
AM-F	169	169	165	165	165	163	158	150	131	112
AM-L	159	159	155	150	145	134	122	104	90	77
DP	160	160	159	158	154	149	141	132	121	104

Comparative efficacy

ASMQ in children: Evaluation of *P. falciparum* recrudescence rate at D63 by PCR in Myanmar



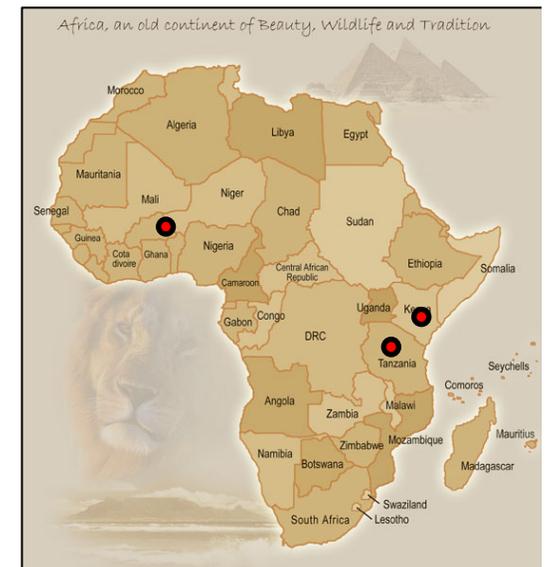
ASMQ in INDIA

- **Phase III study** to assess efficacy, safety and PK of ASMQ FDC in 77 adults with uncomplicated *falciparum* malaria in Goa & Mangalore (ICMR-India)
- **Efficacy** results after PCR correction: 100% at Day 63
- **Safety & tolerability** assessment: 3.9% drug related AEs
No drug discontinuation related to AE
- **Pop. PK:** model developed based on sparse sampling (AS/DHA/MQ)
DHA equivalents $t_{1/2}$: 2.08 Hrs
C_{max} : 1500 ng/ml
MQ $t_{1/2}$: 21.6 days



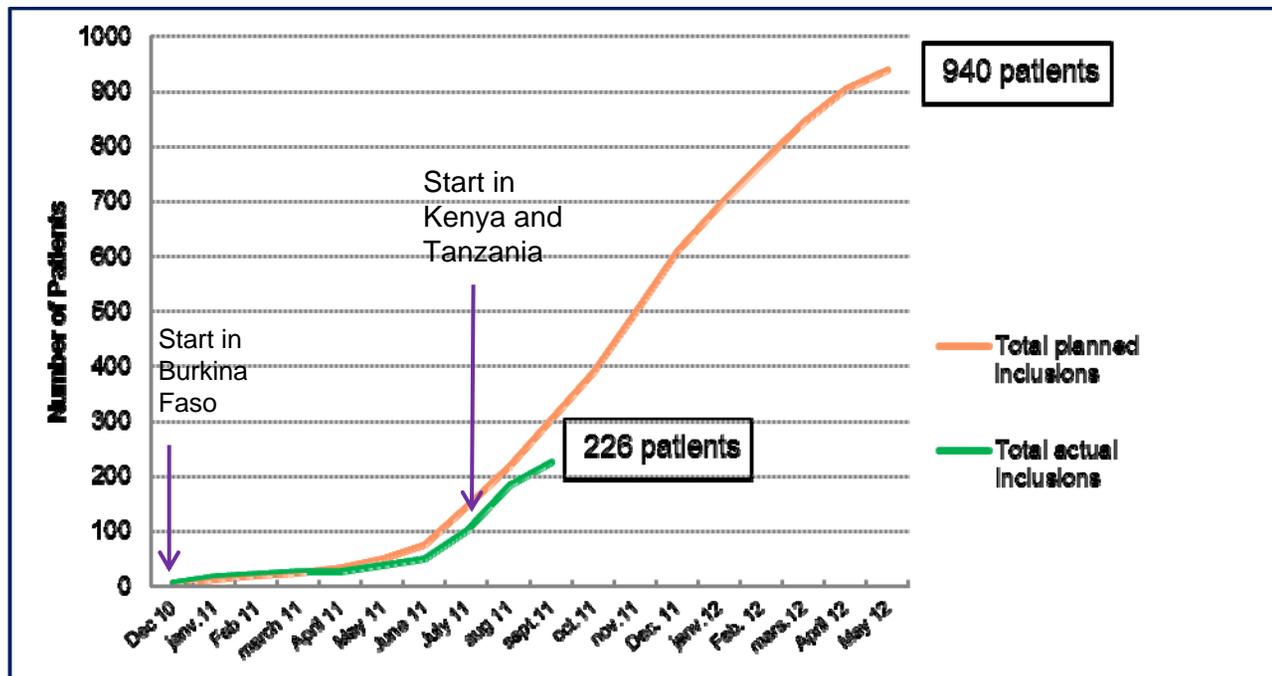
ASMQ in AFRICA

- **Phase IV study** to compare the efficacy and safety of ASMQ fixed-dose combination vs. AL in 940 children under 5 y.o. with uncomplicated *falciparum* malaria
- **Countries:** Burkina Faso (CNRFP), Kenya (KEMRI) and Tanzania (NIMR)
- Supervised 3 days treatment in hospital
- Efficacy trial (cured at D63)
- Safety and tolerability
- Population PK of AS, MQ and Lumefantrine



Progress/ Project Timelines

- **Inclusions curve:**



- **First patient inclusion** : in Q4 2010
- **Last Patient inclusion** : Planned in Q2 2012
- **Last visit of the last patient**: Planned in Q3 2012
- **Results** : Planned in Q4 2012/Q1 2013

ASMQ: Advances & Challenges

From Brazil to Asia and Africa

- Registered by Farmanguinhos in Brazil in 2008 and implemented by the Brazilian national programme
- Donations to Bolivia and negotiations in Peru and Venezuela
- Successful technology transfer to Cipla (India)
- Cipla filing to WHO pre-qualification and Indian/ASEAN registration
- Positioning ASMQ
 - Clinical studies completed: Latin America (Brazil), Asia (India, Myanmar)
 - Clinical studies on going: Africa (Tanzania, Burkina Faso, Kenya), Asia (Malaysia)

