Pharmacovigilance - Cohort events monitoring studies

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Defeating Malaria Together

MMV
Medicines for Malaria Venture

MMV Portfolio: discovering, developing and delivering innovative products

Research

Lead Gen

- Novartis miniportfolio
- GSK miniportfolio
- Broad/Genzyme miniportfolio
- Pfizer Screening
- sanofi Orthologue screen
- AstraZeneca Screening
- Kinases Monash
- Other Projects 15 Projects

Lead Opt

- Novartis 2 Projects
- GSK 2 Projects
- sanofi 1 Projects
- Anitmalarials St Jude/Rutgers/USF
- Antimalarials Dundee
- DHODH UTSW/UW/ Monash
- Oxaboroles Anacor

Translational

Preclinical

- DSM265 (UTSW/UW/ Monash)
- Aminoindole Broad/Genzyme
- MMV048 (University of Cape Town)
- P218 DHFR (Biotec/Monash/LSH TM)
- Pyrazoles (DrexelMED/UW)
- ELQ-300 (USF/OHSU-VAMC)

Phase I

- GNF156 Novartis
- Actelion ACTXXX

Phase IIa

- OZ439 (Monash/UNMC/ STI)
- NITD609 Novartis

Development

Phase IIb/III

- Azithromycin chloroquine Pfizer
- Tafenoquine GSK
- Pyramax Paediatric Shin Poong/University of iowa
- Eurartesim® Paediatric sigma tau

Registration

Phase IV

- Coartem®-D Novartis APPROVED
- Pyramax Shin Poong/University of Iowa APPROVED
- Artesunate for injection Guilin APPROVED
- Eurartesim® sigma tau APPROVED
- ASAQ Winthrop sanofi /DND APPROVED
- SP-AQ Guilin APPROVED

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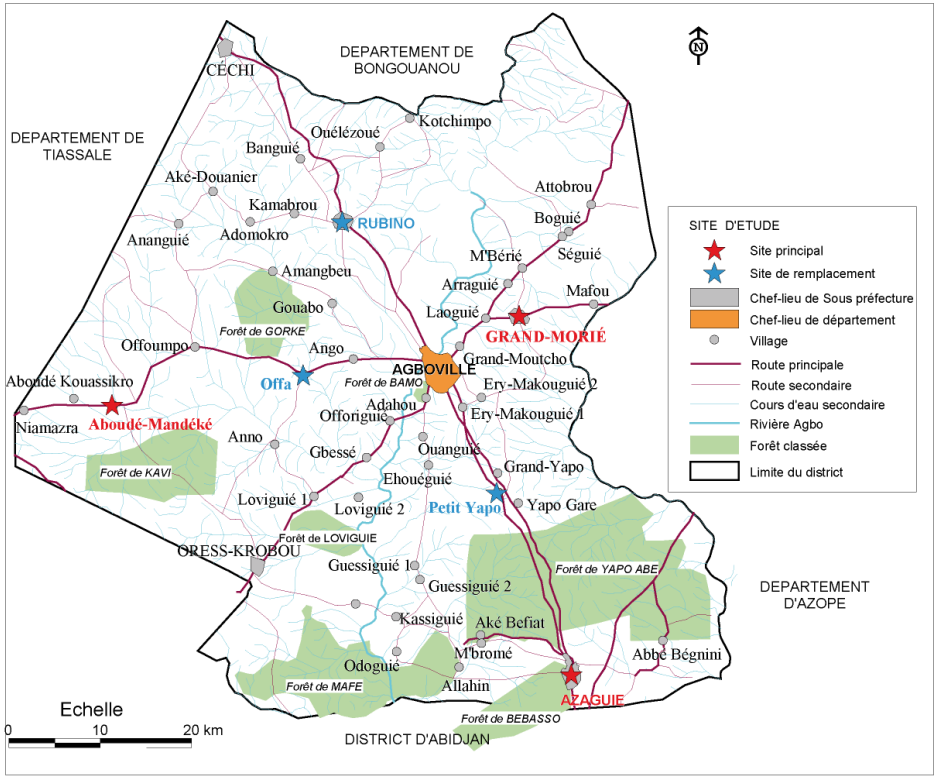
Implementation-safety study with ASAQ in Côte d'Ivoire

- Collaboration with Sanofi and DND*i* in the district of Agboville
- **Implementation-safety study** in 15,000 patients to enable, with a 95% likelihood, the detection of an adverse event occurring with a rate of 1/5000 (classified as "rare" adverse event)
- End of January 2013:
  - 13,018 patients recruited,
  - 85 SAEs reported,
  - signal detected and SmPC updated: extrapyramidal symptoms
  - between 10 and 40 % of the patients reporting AEs to Community Health Workers



⬇ Abidjan 50 Km

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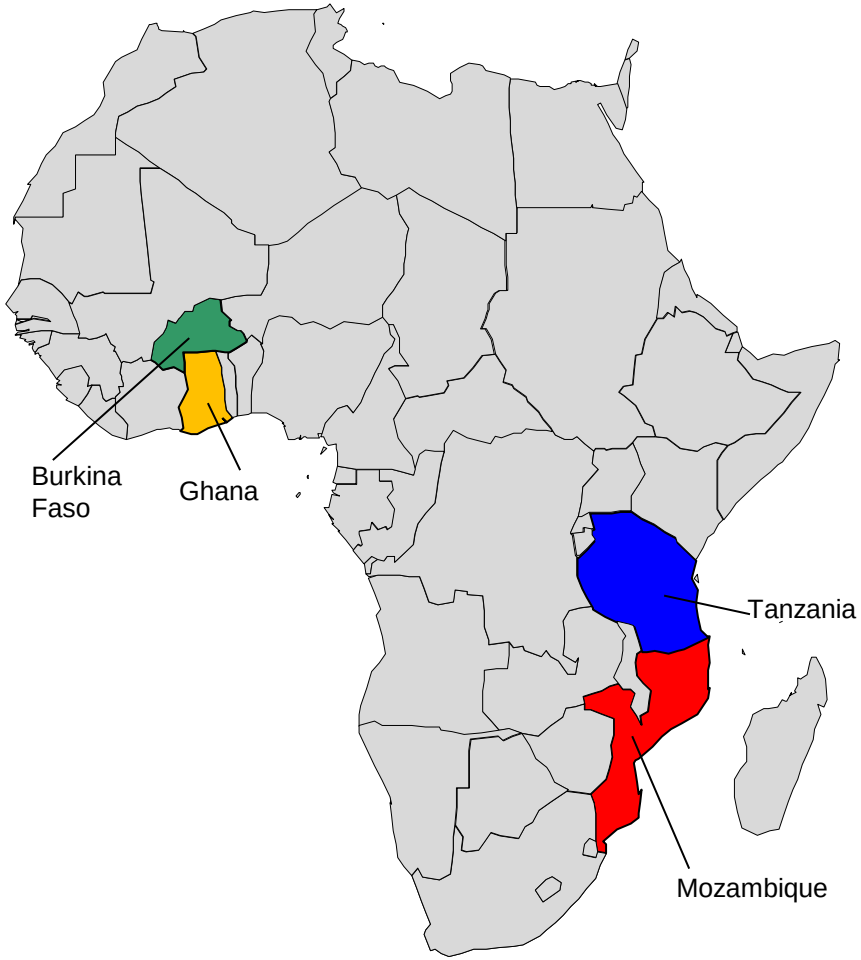
Implementation-Safety (INESS) Study with Eurartesim® (DHA-piperaquine)

- Collaboration with Sigma-Tau and INESS in Tanzania, Mozambique, Burkina Faso, and Ghana
- **Implementation-cohort event monitoring study** in 10,000 patients to enable, with a 95% likelihood, the detection of an adverse event occurring with a rate of 1/3,000 (classified as "rare" adverse event): *safety focused on cardiotoxicity and QT*
- Registration granted in Ghana in January 2013, study expected to start in Q2 2013



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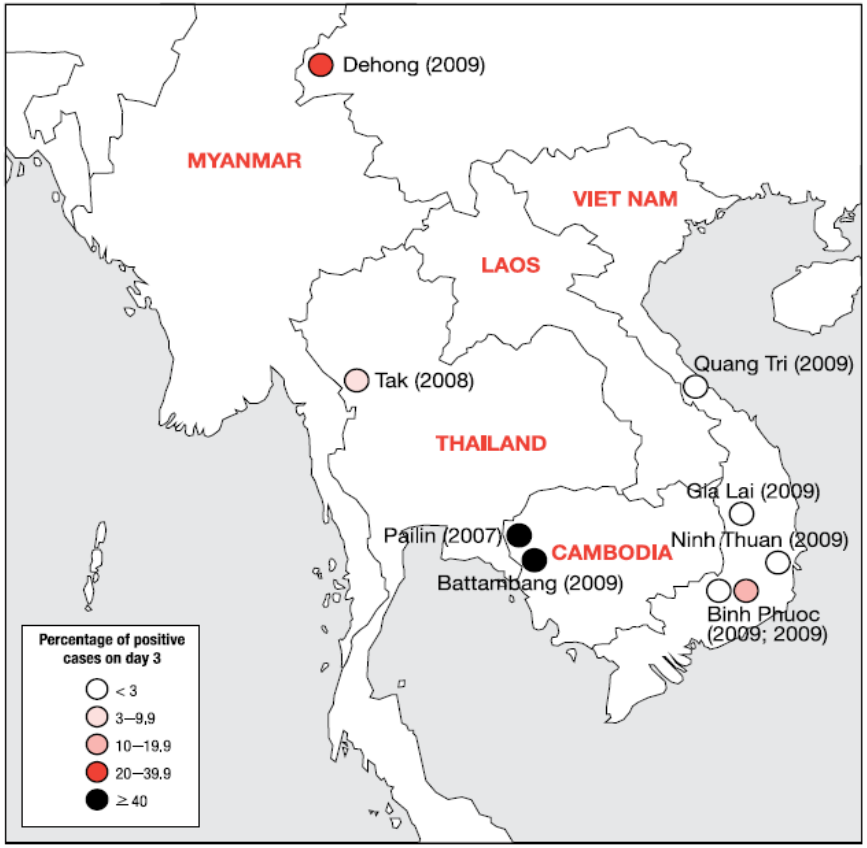
Implementation-Safety Study with Pyramax® (pyronaridine/artesunate) in the Mekong

- Collaboration with Shin Poong and WHO in Western Cambodia and Eastern Thailand
- **Implementation-cohort event monitoring study** in 3,000 patients to enable, with a 95% likelihood, the detection of an adverse event occurring with a rate of 1/800 to 1/1,000 (classified as “uncommon” to “rare” adverse event): *safety focused on hepatotoxicity*
- Protocol in development

Percentages of patients with *P. falciparum* parasitaemia on day 3 after treatment with oral artesunate monotherapy (2–4 mg/kg body weight per day), 2007–2009



The map shows the results of the most recent therapeutic efficacy study per site and per drug only.

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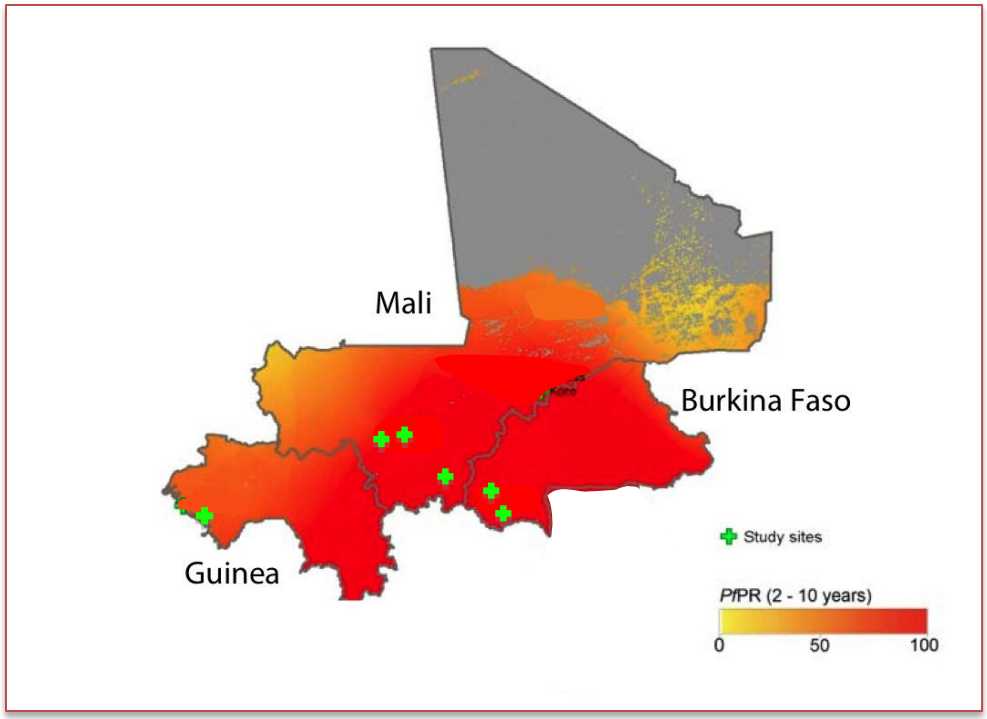
EDCTP Longitudinal Repeat Dose Study

- Phase IIIb/IV randomized, comparative, open, multi-centre study of the safety, efficacy, and impact of repetitive treatment with four artemisinin-based combination therapies (AS-PYR (*Pyramax*), DHA-PQP (*Eurartesim*), AS-AQ, and AR-L) on the incidence of uncomplicated malaria in children
- This design will clarify the safety profile of *Pyramax* and *Eurartesim* in a context similar to large-scale deployment of these new drugs in sub-Saharan Africa
- Study started in October 2011
- January 2013, hepatic safety IDMC review of 59 patients retreated at least once with Pyramax:
  - No difference between first and following treatments
  - No difference compared to the safety profile observed during the development of Pyramax



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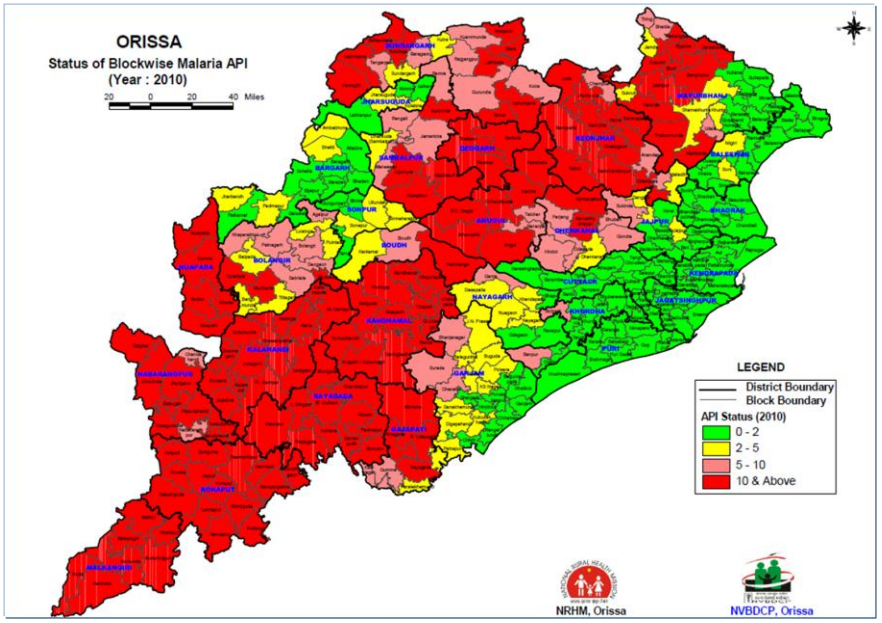
Effectiveness and Cohort Event Monitoring with AS-SP in Orissa, India

- **Collaboration MMV, NIMR and NVBDCP**
- **Effectiveness and cohort events monitoring study in the region of Orissa**
- **Treatment:**
  - AS+SP + Single-dose PQ for *P. falciparum*
  - CQ+ 14 day PQ for *P. vivax*
- **Then in collaboration with DND*i*: AS-AQ, AS-MQ and DHA-PQP?**
- **Programme should start in June 2013**



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Injectable artesunate

- 19 cases of delayed hemolysis reported in five publications with the Guilin injectable artesunate
- One anecdotal report with the WRAIR injectable artesunate
- Meeting on 19 March in Vienna to discuss:
  - reported cases,
  - data from SEAQUAMAT, AQUAMAT and SMAC,
  - possible mechanism of action and
  - next steps:
    - amendment to the current implementation protocol on-going in DRC, weekly hematological follow-up until D28 added to the initial protocol
    - cohort event monitoring study with Swiss TPH in Central Africa (DRC, CAR, Congo, Gabon, Cameroon, Chad)
    - severe malaria registry in hospitals from West and East Africa

THANK YOU

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