Collaborating on Phase IV studies

Registration and beyond

Changing Landscape

- Between 2008-2010 as many as four fix dose ACT from the MMV pipeline
- Many drugs entering into national policy
- Increasing widespread use
- Gap between sponsors and policy

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What is in Phase III

- Artemether – Lumefantrine (AL) – Novartis
  - 62 million treatments delivered in 2006
  - pediatric formulation of Adult form registered in 1999
  - New formulation: dispersible tablet
  - Palatability study, PK study (healthy volunteers) and Phase III trial vs. crushed tablet (890 pediatric patients)

- Dihydroartemisinin – Piperaquine (DHA-PIP) - Sigma Tau, Holley, Oxford University
  - Chinese and Vietnamese versions widely used in SE Asia + numerous publications (3,500 patients exposed)
  - Adult and pediatric formulation
  - 3 PK studies (healthy volunteers, children with malaria and adults with malaria)
  - Two pivotal studies – one in African children (1500) and one in Asia adults (1150)

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What is in Phase III

- Chlorproguanil-dapsone-artesunate - GSK
  - Chlorproguanil-dapsone registered as LapDap with the MHRA and registered in 14 African countries (low uptake)
  - New comibination: LapDap with artesunate
  - Phase I trial (38) Phase II trial (340)
  - Two phase III trials: vs Artemether-Lumefantrine (1395) and vs Chlorproguanil-dapsone (900)

- Pyronaradine-Artesunate – Shin Poong
  - Pyronaradine is a known Chinese antimalarial devoloped in the 1970s with a few trials in Africa.
  - Pyronaradine-Artesunate: Phase I trial (125), 2 Phase II trial (477 and 60)
  - Three phase III trials, one vs. Artesunate +Mefloquine (1269) vs. Artemether –Lumefantrine (1269) and one for P. vivax vs. Chloroquine (456)

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What do sponsors want in Phase IV?

Label extensions – defining the profile of the drugs – usefulness in:

Replacement first line for uncomplicated Plasmodium falciparum

Second line rescue therapy

Follow-on treatments for severe disease

Treatment of malaria in pregnancy

IPTp -IPTi - iPTc

Use in complex emergencies/displaced populations

P.vivax

Travellers' indications (travel and treat)

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Conclusions of the Phase IV meeting

Amsterdam March 5, 2007

- Sixty invited participants – Consortia, WHO, EDCTP, Academia and Industry
- Diverse “immediate” needs lead to the formation of operational evidence generating “consortia”
- Funding remains a major issue
- Consortia play a major role in special areas:
  - ACT Consortium (broad aspects of ACTs)
  - Malaria in pregnancy (MIP)
  - IPTi Consortium
  - Phase IV Consortium (in the process of being defined) – Pharmacovigilance

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Conclusions of the Phase IV meeting

- The Consortia will play a role in collecting/compiling of evidence for national and international malaria policy decisions
- Not all “needs” are covered by existing consortia or organizations (vivax, severe malaria, emergency intervention)
- Consortia do not have the means or expertise of developing tools (e.g. drugs) – mainly academics in the field
- Funding is not yet secured for the various initiatives

- **Highest priority for post registration study is drug safety especially for new drugs**

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Phase IV meeting – Role of MMV moving forward

- MMV will interact with the consortia to identify and create tools where needed:
  - identify if current drugs in its pipeline might be useful for specific interventions
  - develop new drugs for specific needs
  - Work with sponsor in Phase IV and drug safety studies

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MMV's added value in Phase IV

- MMV has a unique relationship with regulators and industry which is not there in the policy makers and consortia
- MMV can act as an advocate for the needs of its partners in the consortia while contributing to the activities of the research community

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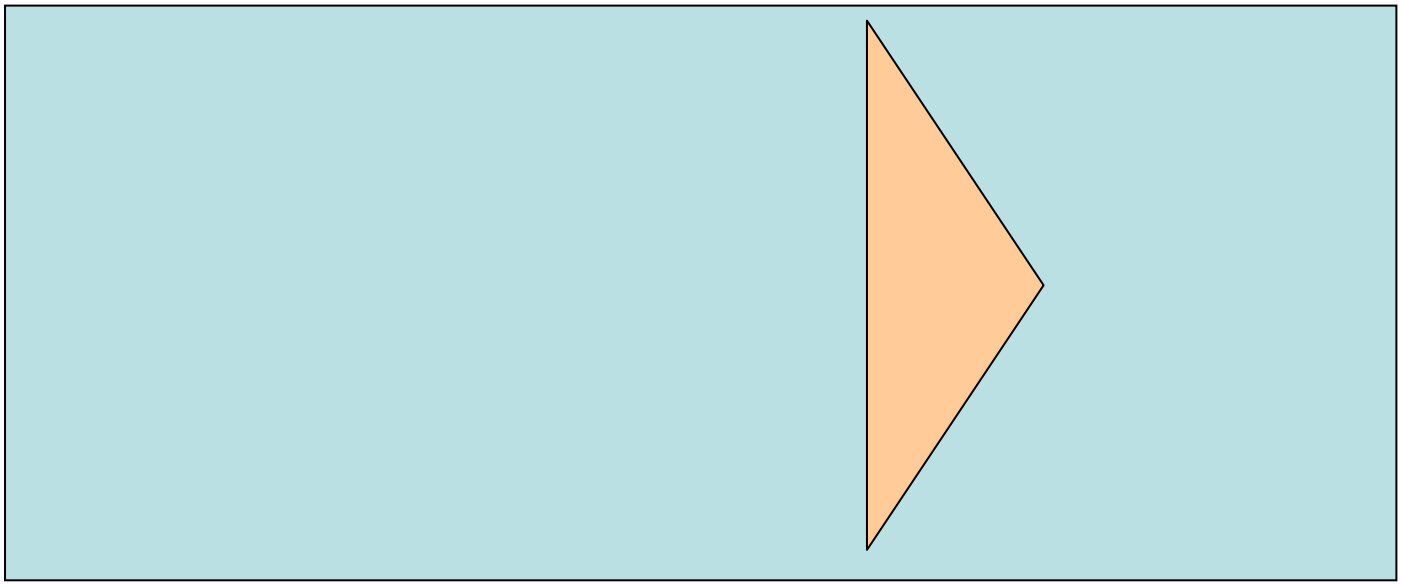
Thank you

Registration and beyond



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