Towards the future: medicines and the elimination of malaria

Defeating Malaria Together

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Chief Scientific Officer MMV
Coartem-D (Novartis) has treated 65 million children so far.
150 million treatments of fixed dose ACTs delivered in 2010.
Adult medicines for un-complicated malaria

- Resistance is a fact of life
- Not all medicines work in all populations
- Different risk-benefit profiles – allows choice

- DHA-piperaquine (sigma-tau)
  - EMA decision expected August 2011
- Pyronaridine-artesunate (Shin-Poong)
  - EMA decision expected 1Q’2012
New child friendly medicines

- Pyronaridine-artesunate granule formulation – submission early 2012
- DHA-piperaquine: taste-masked dispersible formulation - submission late 2012

- Coartem-D: child-friendly formulation: extend to available < 5kg babies
Severe Malaria

- Aquamat artesunate superior to quinine: 5000 patient study
- Guilin first prequalified (Dec 2010) with MMV’s support
- Only Chinese manufacturer with WHO approval
- Cost: approximately $1 per vial
Protecting expectant mothers

• Neither azithromycin nor chloroquine are optimal on their own
• Synergy: azithromycin blocks chloroquine resistance clinically
• 60% of mothers have bacterial infections (STI): impact on peri-natal mortality
• Both drugs treat both diseases
• New fixed dose formulation (Pfizer)
Stopping the relapses from *P. vivax*

- 100 million patients annually
- Hypnozoites: relapse without reinfection
- Gold standard: Primaquine 14 days, G6PD liability
- Tafenoquine (WRAIR, GlaxoSmithKline)
- Pivotal Phase II/III starts 2Q 2011
- Single dose
  - Efficacy
  - Safety

Thanks to Ric Price
Powering the single dose cure: OZ439

- OZ439 collaboration: MMV, Monash, Basel and Nebraska
- Same warhead, different scaffold
- High plasma concentration 48–72 h
- Active in ‘resistant malaria’?
- Currently being tested in patients (phase IIa)
New medicines driving eradication

- Efficacy: No cross resistance or resistance induction, fast killing
- Safe: High therapeutic margin; no serious toxicity
- Long time above the IC\(_{90}\) in plasma
- Low predicted human dose

- Transmission-blocking
- Relapse- blocking
- Chemoprevention
Next generation: guided by structure

- Rapid progression with validated targets

Next generation: guided by Biology

**Chemistry:**
All available molecules

**HTS**
Whole parasite

**Hits to leads**
Identify resistance

- Screening five million compounds
- 25’000 hits < 1 uM
- Fast track to man – less than four years

- *Now let’s look at the other stages: transmission blocking and liver stages*

Wells TNC Science 329 1153-1154 (2010)
Clinically characterise products ‘active in man’
Show ex-vivo activity of plasma, then purify

Natural products as starting points for future anti-malarial therapies: going back to our roots?
Wells TN Malaria Journal 2011, 10(Suppl 1):S3
Miniportfolios – built on chemistry

- New Hits to leads model
- Dedicated teams: medicinal chemists, cell pharmacology
- Partnering in disease endemic countries
  - India
  - South Africa
- MMV experienced Mentors
- Common *in vivo* centres of excellence
MMV’S OPEN ACCESS MALARIA BOX

COMING SOON: FREE SAMPLES OF 400 DIVERSE COMPOUNDS WITH ANTIMALARIAL ACTIVITY TO BE MADE AVAILABLE BY MMV AND SYNEKIS IN Q4 2011

This potential treasure trove of compounds, selected from publically available hits, will be a resource to catalyze malaria drug discovery and research. It includes:

- 200 diverse “drug-like” compounds as starting points for oral drug discovery and development
- 200 diverse “probe-like” compounds for use as biological tools in malaria research

Available Autumn 2011
Further details malariabox@mmv.org
Delivering game changing molecules

NITD609 (Novartis): new class, phase Ila 4Q’11
AN3661 (Anacor): fast acting, potent, safe. phase I 4Q’11

GNF156 (Novartis): liver schizontocide, phase I 1Q’12

New candidates
2011  Aminoindole (Genzyme) no in vitro resistance
      DHODH inhibitors (DSM, Genzyme, GSK)
2012  new series: fast killers
      new series: liver stages
      new series: transmission blocking
      new series: stage 4, 5 gametocytes

… targeting the eradication agenda
Thanks to all our colleagues and partners – but especially to the children and their families who make the next generation of malaria therapy a reality.
Today’s agenda

• *New medicines for protection during pregnancy* Dr Joshua Kimani KEMRI Kenya

• *DHA/PQP: a new once-per-day treatment for uncomplicated malaria* Dr Ambrose Talisuna WWARN East Africa

• *Artesunate for injection: new evidence for the management of severe malaria* Dr Antoinette Tshefu University of Kinshasa, DRC

• *DHODH: structure based design of a new class of drugs* Dr Margaret Philips University of Texas Southwestern USA

• Panel discussion: chaired by Dr Bernards Ogutu and Dr Timothy Wells