Intermittent screening with rapid diagnostic tests and treatment with Dihydroartemisinin-Piperaquine for malaria in pregnancy: An individually pooled analysis

STOP-MIP (Kenya) & ISTp-Malawi (Malawi) Trials
Intermittent Screening and Treatment in Pregnancy: Concept

• Provides scheduled screening for malaria using a malaria rapid diagnostic test (mRDT) and treating mRDT-positive women with a long acting ACT

• Ensures that only women with detectable malaria infection receive treatment

…… malaria infection heterogeneity in local geographical areas

• Clears existing infections

• Provides additional post-treatment prophylaxis for up to six weeks
Promising preliminary study from West Africa

• ISTp-AQ-AS non-inferior to IPTp-SP (2007-8)
  Moderate to high malaria transmission
  Low prevalence of SP resistance (K540E <1%....2010-11)

• ….potential of strategy in areas with high SP resistance
Pooled results of two ISTp-DP trials……

STOPMIP (Kenya) - 2012
IPTp-SP vs. ISTp-DP vs. IPTp-DP

ISTp-Malawi (Malawi) - 2011
IPTp-SP vs. ISTp-DP
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Study overview

• Design
  – Open-label randomized controlled superiority trials
  – HIV negative women from 16-32 weeks gestation
  – Singleton pregnancies

• Study sites:
  – All women used insecticide–treated bed nets
  – High transmission, high SP resistance

• Malawi: 3 sites southern Malawi
  – Transmission: PfPr 2-10 years, 2010= 0.394
  – Resistance: 100% dhfr/ dhps quintuple mutant; 1.5% Pfdhps-A581G (sextuple)
  – Sample size: 1,844, 2 arms (922 per arm)

• Kenya: 4 sites western Kenya
  – Transmission: PfPr 2-10 years, 2010= 0.565
  – Resistance: 96% dhfr/ dhps quintuple mutant; 5.8% Pfdhps-A581G (sextuple)
  – Sample size: 1,554, 3 arms (515 per arm)
Interventions and follow-up schedule

• Interventions:
  
  **IPTp-SP arm**: 3 tablets SP (500mg/25 mg), stat
  **ISTp-DP arm**: HRP-2/ pLDH combo RDT………RDT+, standard 3-day course of DP

• DP: Euartesim, Sigma Tau, Italy, 40mg/320 mg tablets

| Number of tablets administered per dose |
|---|---|---|---|---|
| 2 | 2.5 | 3 | 3.5 | 4 |
| Weight (kg) | Kenya | 24-35.9 | 36-74.9 | ≥75 |
| Malawi | <50 | 50-59 | 60-69 | ≥70 |

Kenya: Drug dosing based on weight at enrollment
Malawi: Drug dosing based on weight at time of dosing

• Samples: **RDT** (ISTp routinely, IPTp only at delivery); **Microscopy** (maternal peripheral blood, placental incision, cord); **PCR**; **Haemoglobin** (last ANV); **Placental histology** (delivery)
Summary of findings

• ISTp-DP not superior to IPTp-SP. Associated with:

  Higher risk of any malaria infection at delivery (esp. G3+)
  Higher risk of any malaria infection during pregnancy
  Higher risk of placental malaria
  Lower birth weight in paucigravidae
  Suggested higher risk of any adverse live birth outcome

• However

  DP well tolerated
  Screening and treatment well received by clients and staff
Conclusion

- Results should be equally relevant to other areas in east and southern Africa with similar or lower levels of parasite SP resistance.

- No indication to change policy in non-super resistant settings until viable alternative is found.

- IPTp appears to remain a viable strategy but need for safe and efficacious drug to replace SP

- Urgent investigation of promising alternative(s) required
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