EFFICACY AND SAFETY OF ARTEMETHER-LUMEFANTRINE AND ARTESUNATE- AMODIAQUINE FOR TREATMENT OF UNCOMPLICATED FALCIPARUM MALARIA IN MAINLAND TANZANIA

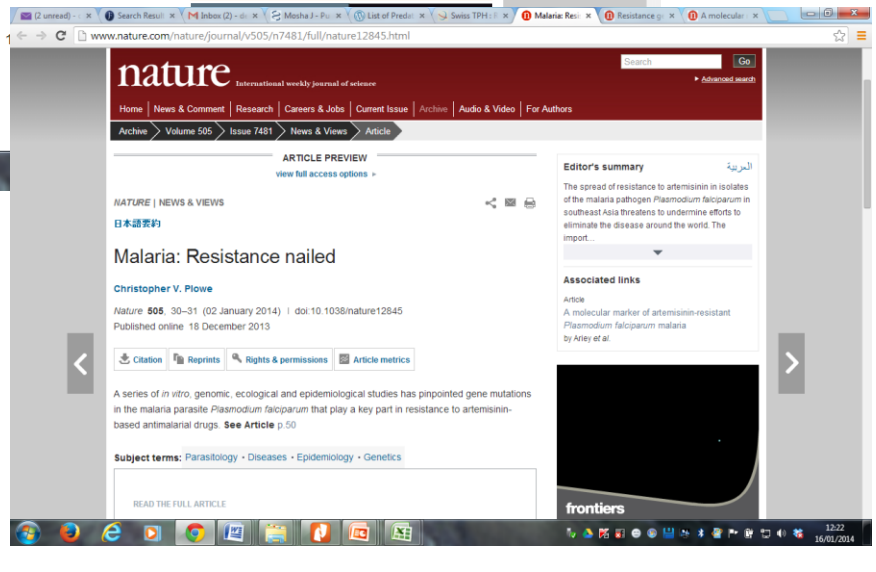
PRELIMINARY FINDINGS INVIVO 2011/2012

D. Ishengoma & TETs Group

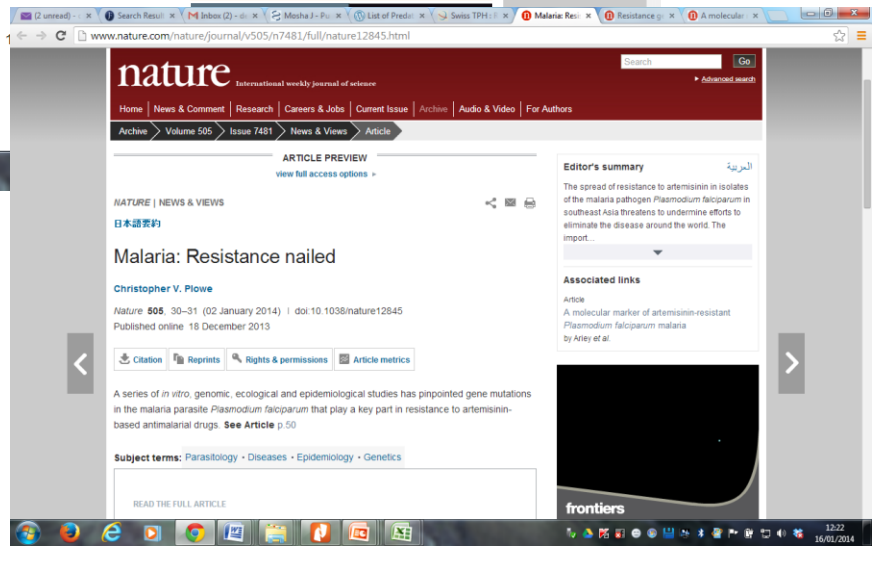
Background

- ALu was introduced Tanzania as first line treatment of uncomplicated falciparum malaria in November 2006 and become fully rolled out in January 2007
- Despite implementation of the new malaria guidelines, TETs were not been fully implemented as recommended by WHO
- Although the efficacy of ALu is still high, there is a threat of ACT drug resistance as recently confirmed in South-eastern Asia
- Thus, monitoring needs to be urgently intensified by NMCP and its partners

Artemisinin resistance



Artemisinin resistance



Objective

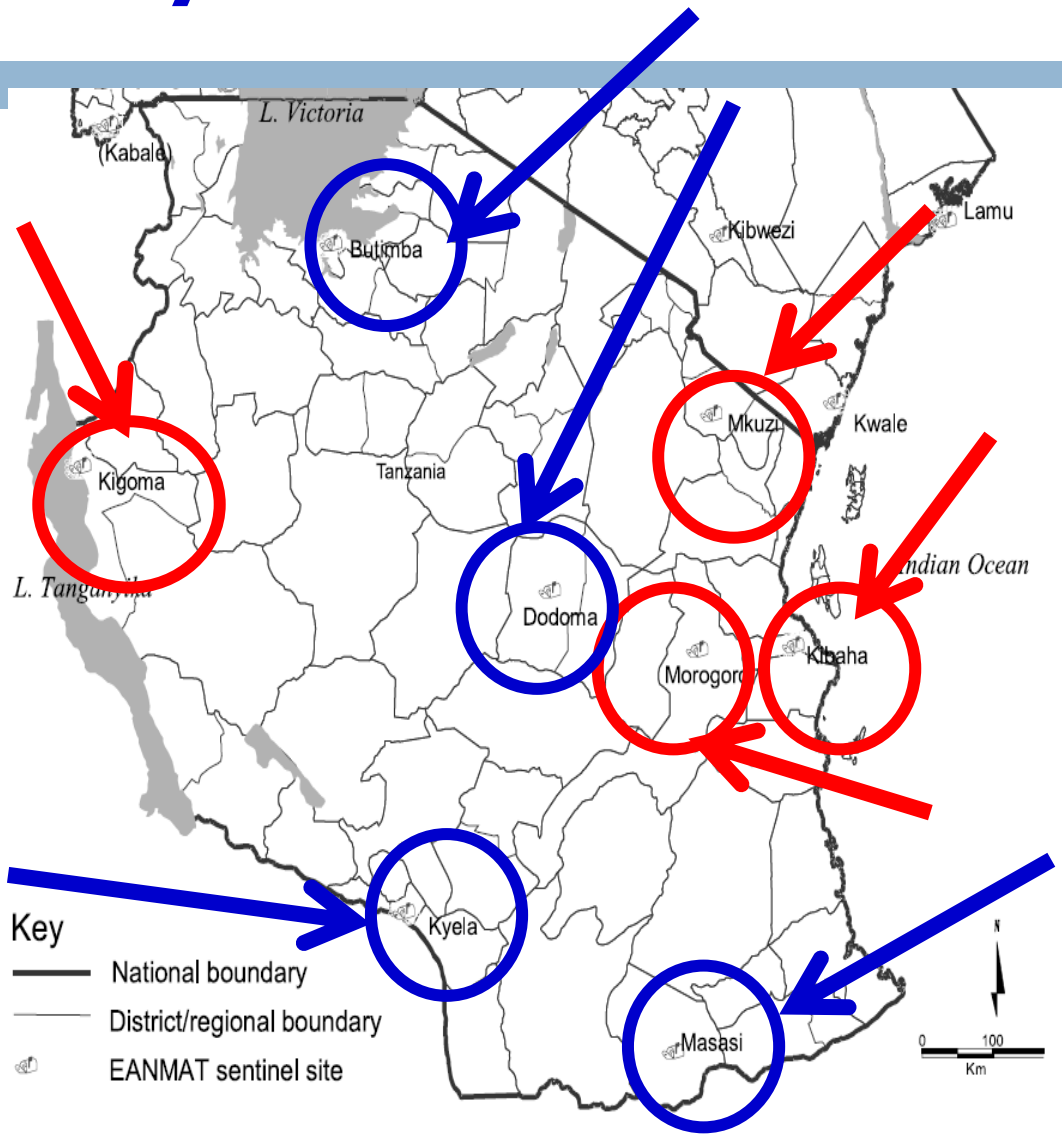
To assess the efficacy and safety of artemether/Lumefantrine (ALu) and Amodiaquie/artesunate (ASAQ) at 8 sentinel sites under NMCP

Methods…1

- Design: open label, single arm in-vivo efficacy studies
- Studies were based on WHO protocol of 2009
- Target:
  - 88 children per site
  - Age
    - In 2011: 6 – 59 months with *P. falciparum* mono-infection + other WHO criteria.
    - 2012: 6 months to 10 years

Methods…2: Study sites

- 8 NMCP Sentinel sites
- 2011 (RED)
  - Mkuzi, Mlimba, Kibaha and Ujiji
- 2012 (BLUE)
  - Butimba, Nagaga (Masasi), Kyela and Chamwino



Methods...3

- Study drugs
  - 2011
    - ALu - Mkuzi and Mlimba
    - AQAS - Ujiji and Kibaha
  - 2012
    - ALu was used at all sites.
- Follow-up: 28 days
- Primary end point :
  - Day 28 cure rates, uncorrected and PCR corrected for recrudescent Vs new infection

Results 1: Invivo 2011…ASAQ

- In 2011-Ujiji-Kigoma

SUMMARY OF CLASSIFICATION PCR-CORRECTED				
	N	Proportional	Lower 95% CI	Upper 95%CI
ETF	0	0.000	0.000	0.073
LCF	0	0.000	0.000	0.073
LPF	0	0.000	0.000	0.073
ACPR	49	1.000	0.927	1.000
Total	49			
WHT	15			
LCF	7	0.310		
Total	71			

- In 2011-Kibaha

SUMMARY OF CLASSIFICATION PCR-CORRECTED				
	N	Proportional	Lower 95% CI	Upper 95%CI
ETF	0	0.000	0.000	0.132
LCF	0	0.000	0.000	0.132
LPF	0	0.000	0.000	0.132
ACPR	26	1.000	0.868	1.000
Total	26			
WHT	1			
LCF	3	0.133		
Total	31			

Invivo 2011… ALu

- 2011 - Mlimba -Kilombero

SUMMARY OF CLASSIFICATION PCR-CORRECTED				
	Number	Proportional	Lower 95% CI	Upper 95%CI
ETF	0	0.000	0.000	0.522
LCF	0	0.000	0.000	0.522
LPF	0	0.000	0.000	0.522
ACPR	5	1.000	0.478	1.000
Total	5			
WHT	0			
LCF	0	0.000		
Total	5			

- 2011 – Mkuzi Tanga

SUMMARY OF CLASSIFICATION PCR-CORRECTED				
	N	Proportional	Lower 95% CI	Upper 95%CI
ETF	0	0.000	0.000	0.119
LCF	0	0.000	0.000	0.119
LPF	0	0.000	0.000	0.119
ACPR	29	1.000	0.881	1.000
Total	29			
WHT	0			
LCF	2	0.065		
Total	31			

2011 - Summary findings...

- Efficacy at all sites was >95%
- No early treatment failure
- Late parasitological failure

  Seven patients.
- Late clinical failure

  Nine patients.
- PCR adjustments

  13 new infections

  2 negative PCR

  1 sample missing

Invivo 2012… ALu (all sites

- In 2012- Chamwino-Dodoma

SUMMARY OF CLASSIFICATION PCR-CORRECTED				
	N	Proportional	Lower 95% CI	Upper 95%CI
ETF	0	0.00	0.000	0.148
LCF	0	0.00	0.000	0.148
LPF	1	0.043	0.001	0.219
ACPR	22	0.957	0.781	0.999
Total	23			
WHT	2			
LCF	1	0.115		
Total	26			

- In 2012- Ipinda – Kyela Mbeya

SUMMARY OF CLASSIFICATION PCR-CORRECTED				
	Number	Proportional	Lower 95% CI	Upper 95%CI
ETF	0	0.000	0.000	0.112
LCF	2	0.065	0.008	0.214
LPF	1	0.32	0.001	0.167
ACPR	28	0.903	0.742	0.980
	31			
WHT	3			
LCF	8	0.262		
Total	42			

Invivo 2012…

- Butimba-Mwanza

SUMMARY OF CLASSIFICATION PCR-CORRECTED				
	Number	Proportional	Lower 95% CI	Upper 95%CI
ETF	0	0.000	0.000	0.459
LCF	0	0.000	0.000	0.459
LPF	0	0.000	0.000	0.459
ACPR	6	1.000	0.541	1.000
Total	6			
WHT	0			
LCF	0	0.000		
Total	6			

- Masasi-Mtwara

SUMMARY OF CLASSIFICATION PCR-CORRECTED				
	Number	Proportional	Lower 95% CI	Upper 95%CI
ETF	0	0.000	0.000	0.074
LCF	0	0.000	0.000	0.074
LPF	0	0.000	0.000	0.074
ACPR	48	1.000	0.926	1.000
Total	48			
WHT	6			
LCF	22	0.368		
Total	76			

2012 - Summary findings…

- Efficacy at all sites was >95% except Kyela
- No early treatment failure
- Late parasitological failure
  - 6 patients
- Late clinical failure
  - 2 patients
- After PCR adjustment
  - 4 recrudescence
  - 3 new infections
  - 1 Negative PCR

General Summary of findings…

- Eight NMCP sites covered into two rounds
  - 2011-Ujiji-74, Kibaha-30, Mkuzi-32 and Mlimba-5
  - 2012-Chamwino -26,Kyela -44,-Nagaga 76 and Butimba-6
- In all sites the enrollment was below except Ujiji and Masasi
- Enrollment between Jun-October.
- Total of 293 children enrolled
  - With drawn 11
  - Lost to follow up 43
- 21 more withdrawn after PCR correction
  - New infections
  - Negative PCR
- 218 patients were analyzed.

Discussion and Conclusion

- Both ALu and ASAQ had very high efficacy
  - The clinical efficacy of ASAQ in previous studies eg. 2007 was relatively higher in areas with high transmission due to high rate of re-infections
- The lack of sufficient cases with malaria parasites was a major problem in both rounds
- New approaches are needed to capture more patients and reach the target sample size.

Way forward 2014/2015

- Conduct a round of testing at 4 sites – from May 2014
  - Three ACTs to be tested – AL, ASAQ and DHA-PQ
- Future studies to include assessment of parasite clearance time to generate baseline data in Tanzania

Challenges for future studies

- Due to declining transmission, extending follow up to 6 months is needed
- Testing 2 ACTs per site

- **Finance:**
  - To extend the study to or beyond 6 months and
  - Testing 2 ACTs at each site
  - Surveillance of PCT (approx. USD120,000 per year)

Acknowledgements

- Partners

- Funders

- District Health Authorities

- Study Participants