Cohort Event Monitoring with Artesunate Amodiaquine at Kintampo HDSS: a unique platform for collection of rigorous safety data on Medicines

Anthony Kwarteng on behalf of INESS team,

October 25, 2011.
CICJC, Maputo

Authors and affiliations

Kwarteng A[1], Asante K P[1], Abokyi L[1], Konadu D[1], Gyaase S[1], Amengo-Etego S[1], Adjuik M[3], Kajungu D[3], Ako-Adounvo S[2], Dodoo A[2], Binka F[3], Owusu-Agyei *S*[1].

1. *Kintampo Health Research Centre, Kintampo, Ghana.*
2. *WHO Collaborating Centre for Advocacy and Training in Pharmacovigilance, University of Ghana Medical School, Ghana*
3. *INESS/ INDEPTH Network*

Background - 1

- Medicine morbidity and mortality is a public health problem globally
  - → Adverse drug reaction (ADR) ranked 4th - 6th leading cause of US death
  - → About 10% of hosp admissions
- Safety data on new antimalarials approaching licensure are often limited
  - Less than 6000 exposures
  - 10 000 exposures to detect rare event in1:3000.
- The situation is worse in resource limited health systems especially developing countries.

Background - 2

- INDEPTH Effectiveness and Safety Studies (INESS) is a new platform for Phase IV studies on new and existing antimalarial treatments
  - 7 HDSS sites across
  - 4 African countries namely GH, MZ, TZ and BF
- The ongoing ACT CEM is hosted on the INESS platform.
- Advantages of the platform
  i. **real life** safety data in **real time**
  ii. known denominators
  iii. opportunity for vaccine safety and other medicines

Study objective

- To determine the incidence of ***adverse events*** related to Artesunate Amodiaquine (ASAQ)

  - **Definition of *adverse event***

Any untoward medical occurrence ***(new or worsening)*** that may present during treatment with a medicine but does not necessarily have a causal relationship.

Study population and area

- **Study Cohort:**
  → Anyone ≥ 6 months prescribed fixed or loose dose ASAQ
  → For treatment of suspected or proven uncomplicated *falciparum* malaria

- **Study area:**
  → Private and public health facilities
  → HDSS population of Kintampo North and Kintampo South in the middle belt of Ghana
  → Resident population of 140,000

Study design and procedure

- Prospective non-interventional observational study
- All patients prescribed ACTs were enrolled by trained health workers after written informed consent.
- Data being presented is on ASAQ
- Patients enrolled were identified on the HDSS platform and followed up 3-7days by trained field supervisors
- Data on presenting signs and symptoms, malaria diagnosis, presence or absence of AEs were recorded.
- Completed pre- and post-treatment forms were reviewed by pharmacists and clinicians and suspected drug(s) if any indicated.

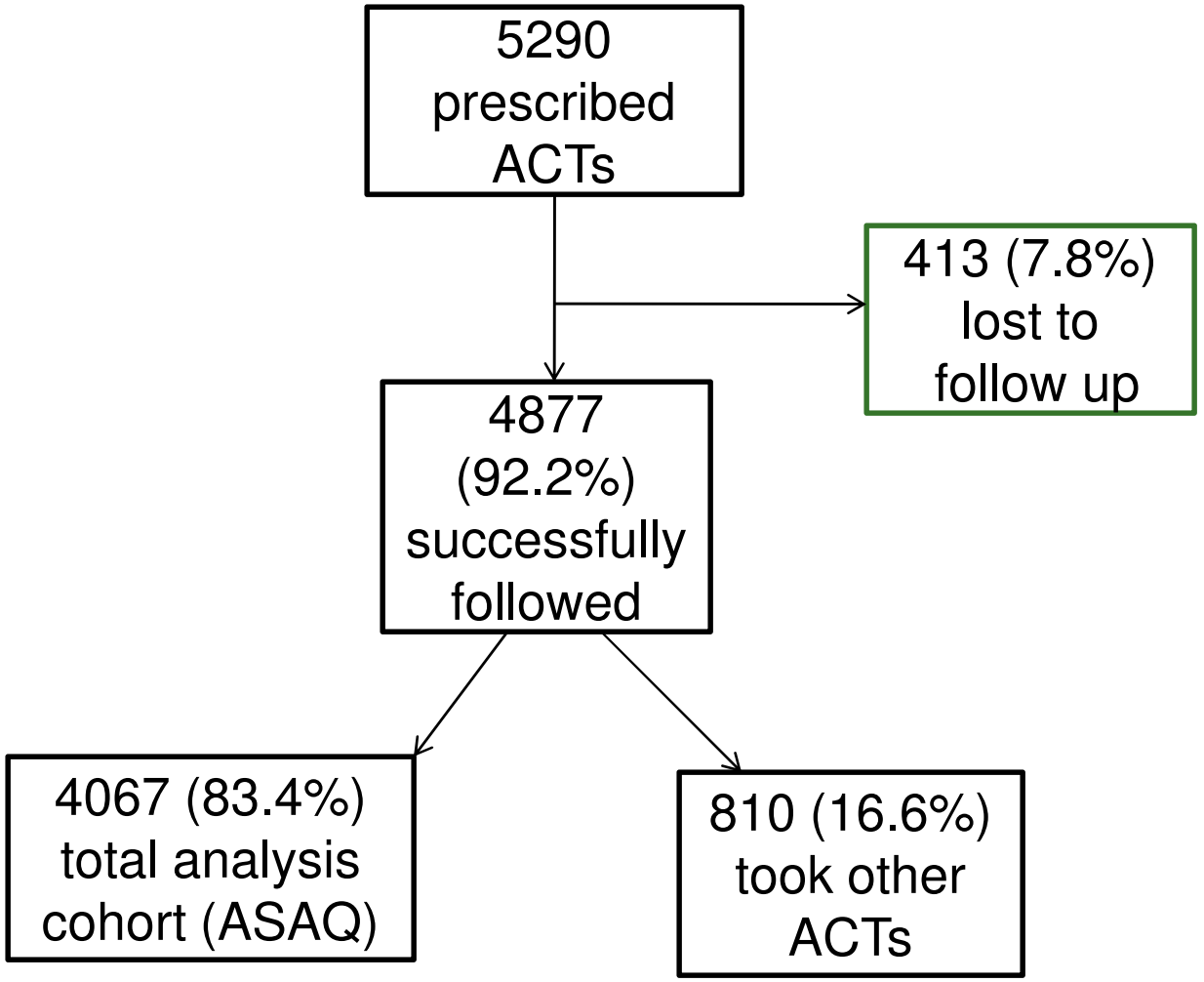
Findings

Characteristics of patients who took ASAQ by age and sex

N =4067

Parameter	Freq (n)	Percentage (%)
Age		
< 5	1960	48.2
5 – 9	642	15.8
10 – 14	286	7.0
15 – 19	110	2.7
≥ 20	1069	26.3
Sex		
Male	1709	42.0
Female	2358	58.0

- **11.6%(8/69) of pregnancies were unintentionally exposed to ASAQ**
- **35.9% (1459/4067) of patients were tested for malaria prior to tx**



Details of enrollment and follow up

Looking at the incidence

- 1138 out of 4067 study participants reported at least one adverse event (28.0%; 95%CI,0.26 – 0.29)
- The 1138 individuals reported a total of 1754 adverse events
- 632 of 4067 participants had at least one AE related to ASAQ. (15.5%; 95% CI, 0.15 – 0.17)
- 989 out of 1754 adverse events reported were related to ASAQ (56.4%; 95% CI, 0.54 – 0.59)

Incidence of adverse events (ASAQ related) in patients who took either fixed and loose dose

ASAQ type	ASAQ type taken	Adverse event n (%)	Incidence (%)
Fixed dose	1923	511 (51.7)	**26.6**
Loose dose	2144	478 (48.3)	**22.3**
Total	**4067**	**989 (100)**	

Top ten most occurring ASAQ-related adverse events among participants exposed.

No	Adverse event	Frequency (n)	Percentage (%)	95% CI
1.	Weakness	143	14.5	0.12 – 0.16
2.	Stomach ache	89	9.0	0.07 – 0.11
3.	Dizziness	84	8.5	0.06 – 0.11
4.	Vomiting	82	8.3	0.06 – 0.11
5.	Headache	69	7.0	0.05 – 0.09
6.	Loss of appetite	66	6.7	0.05 – 0.09
7.	Fatigue	57	5.8	0.04 – 0.06
8.	Drowsiness	46	4.7	0.03 – 0.05
9.	Fever	42	4.3	0.03 – 0.05
10.	Diarrhoea	41	4.2	0.03 – 0.05

Incidence of Serious adverse events among the cohort

N =4067

SAE	Frequencies	Percentage (%)
Hospitalization	3	0.0737
Life threatening	3	0.0737
Disability	1	0.0246
Death	1	0.0246
Total	**8**	**0.1967**

Experiences of CEM in KHDSS

- The awareness about CEM has improved spontaneous reporting within the routine health services
- Trained staff (both projects and in health facilities) who report and refer AEs to the study team
- Strategies now in place for follow-up
  - → Using phones
  - → Simplified case report form
- Established linkage b/n DSS and routine HF data that will potentially provide baseline health indices useful in interpreting signals

Conclusions

- The use of ASAQ is related to common adverse events similar to those reported during Phase III studies.

- The HDSS provides an excellent opportunity for collection of rigorous safety data on medicines in real life setting in Africa.

Acknowledgements

- The staff of Kintampo Health Research Centre
- WHO Collaborating Centre for Advocacy and Training, University of Ghana.
- The Ghana Food and Drugs Board
- INDEPTH Network
- Bill and Melinda Gates Foundation

Thank you