

Efficacy of Artemether- lumefantrine in children Admitted for Malaria of Moderate Severity

P. Sasi, M. English, S. Muchohi, M. Makanga, G. Kokwaro

KEMRI/Wellcome Trust Research Programme



wellcome**trust**



Background

- Clinical malaria is commonly described as mild or severe
- Most children admitted for malaria have no features of severe disease
- No treatment guidelines, in practice treated with parenteral quinine
- Most can tolerate oral medication and use of quinine may be wasteful and potentially dangerous

Background continued

- Oral artemether-lumefantrine may be a beneficial alternative
- However, lumefantrine bioavailability might be a potential problem
- Lumefantrine AUC determines cure and day 7 lumefantrine below 280ng/ml -in vivo MIC for multi-drug resistant parasites - increased risk for treatment failure

Objective

- Assess efficacy of Coartem[®] in children with moderate malaria
- Investigate lumefantrine bioavailability using day 7 plasma lumefantrine as a surrogate of AUC

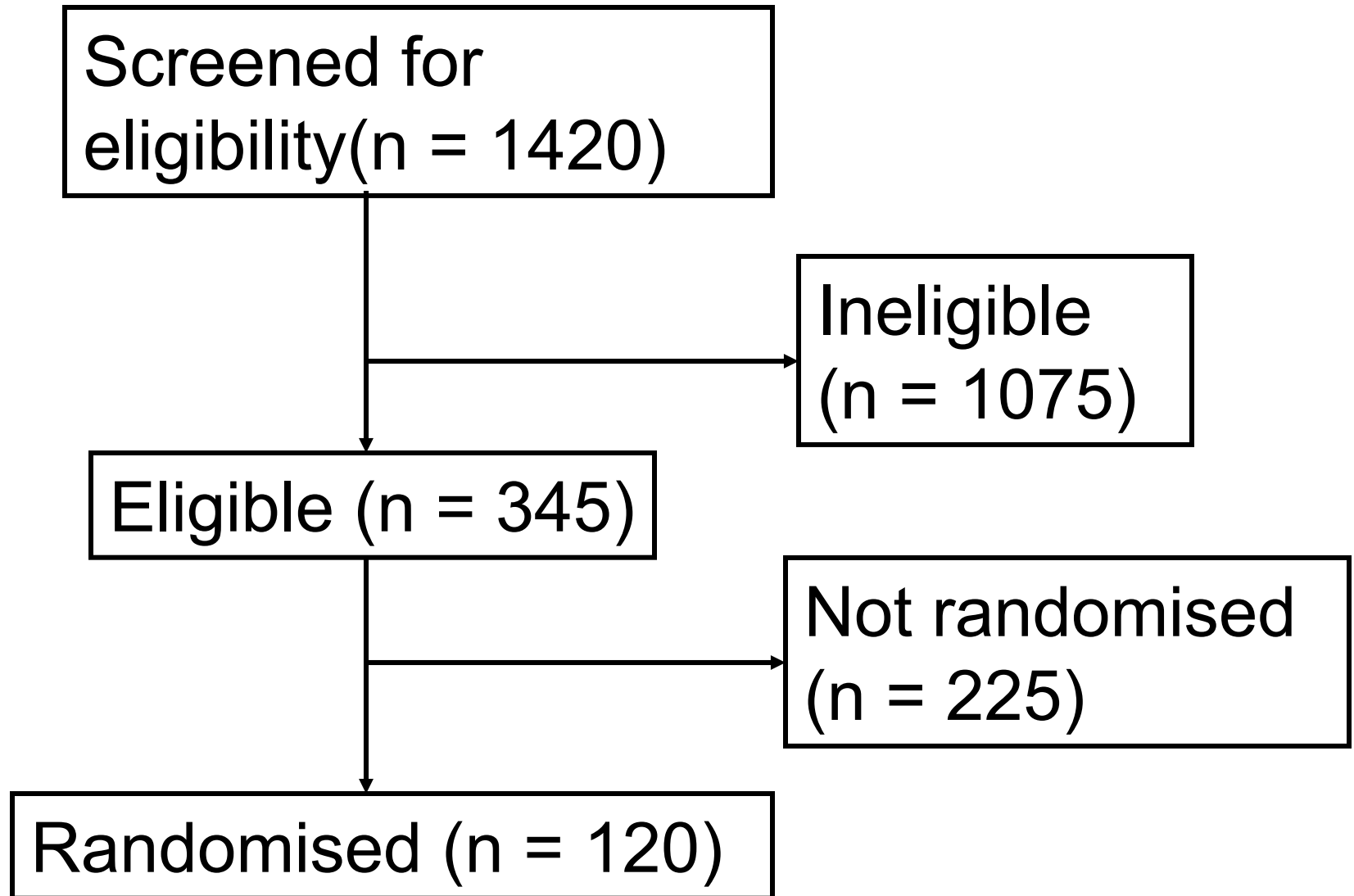
Study Methods

- Open label RCT with SP as comparator in children admitted to KDH with moderate malaria
 - Age 6 months to 13 years
 - Weight \geq 5kg
 - Confirmed *P. falciparum* 2000 per μ l or more
 - No signs of severe disease
 - No other illness or cause of fever

Study Methods continued

- Daily clinical assessment for efficacy and AE during treatment
- Active follow-up – day 7, 14 and 28
- Plasma for lumefantrine on day 7 in Coartem[©]-treated children
- Kenya adopted Coartem[©] as first line treatment before trial completion

Trial Profile



Treatment Response - preliminary

Fansidar[®] Coartem[©] Coartem[©]
overall

ETF

ITT 15/62(24%) 3/52(6%) 4/113(4%)

PP 10/57(18%) 1/49(2%) 1/110(1%)

Day14ACPR

ITT 34/63(54%) 44/52(85%) 96/113(85%)

PP 34/45(76%) 44/46(96%) 96/99(97%)

Day28ACPR

ITT 21/63(33%) 36/52(69%) 76/113(67%)

PP 21/36(58%) 36/44(82%) 76/98(78%)

Day 7 lumefantrine levels in Coartem[®] - treated patients (n = 113)

Data available	99 (88 %)
Mean (95 % CI)ng/ml	236.9 (129.8 –344.8)
Less than 280ng/ml	57 (51 %)

Conclusions

- Efficacy of Coartem[®] in moderate childhood malaria is comparable to that in uncomplicated malaria
- The putative lumefantrine in vivo MIC is not achieved on day 7 in up to 50% of children despite acceptable efficacy

Acknowledgement

Study participants and
parents

All staff KEMRI CGMRC

- J. Nokes
- K. Marsh
- N. Peshu
- G. Kongola

- M. Temu
- G. Rimoy

Funding

- MIM/ WHO TDR
- Wellcome Trust



wellcome trust

