PREGACT

The safety and efficacy of four artemisinin-based combination treatments in pregnant African women with malaria

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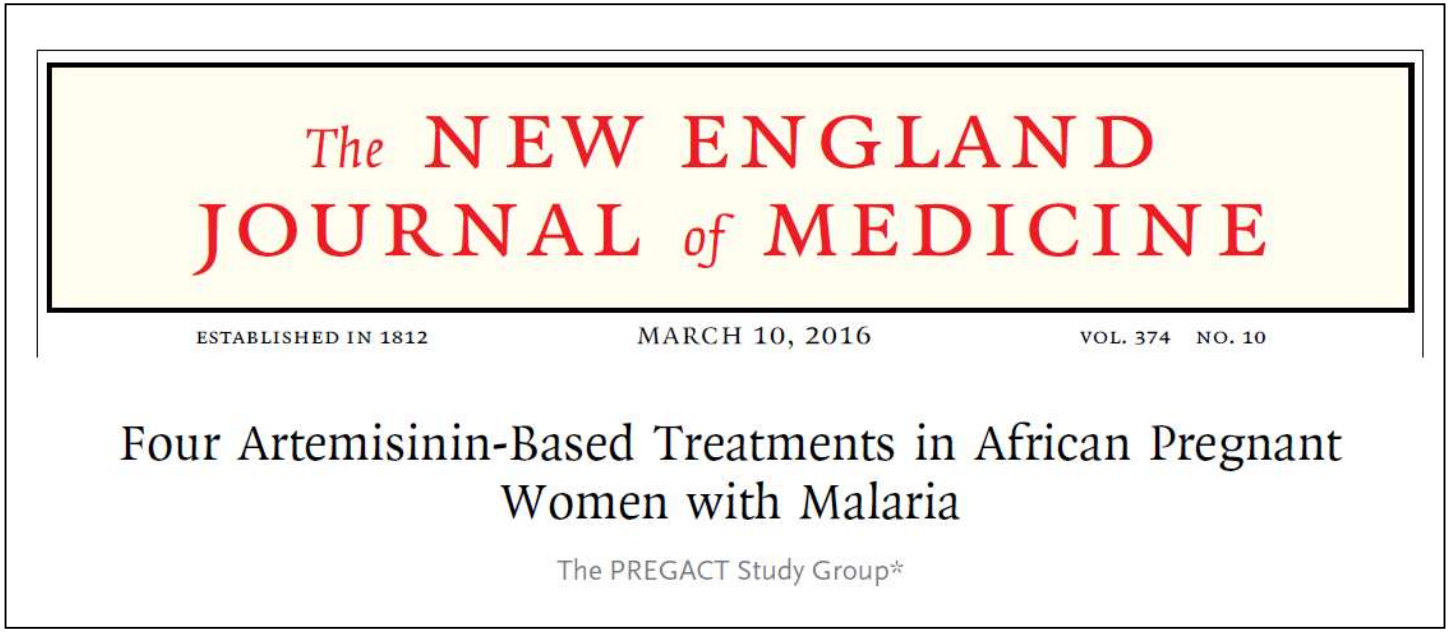
Background

- Malaria in pregnancy is a major public health concern
- If asymptomatic Increased risk of maternal anaemia and low birth weight -> increased infant mortality
- If symptomatic increased risk for fetal loss and maternal death
- Prevention and treatment required
- Limited treatment options
- WHO recommendation for ACT in 2nd and 3rd trimester
- Limited information on safety and cures rates



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Four Artemisinin-Based Treatments in African Pregnant Women with Malaria

The PREGACT Study Group*

Largest ever clinical trial on malaria during pregnancy in Africa
Results of study involving over 3000 women in Burkina Faso, Ghana, Malawi and Zambia

Design

- Multicentre, randomised, open label;
- 4 ACTs tested: AL, AQAS, DHA-PQ and MQAS, with 3 arms in each centre (balanced incomplete block-design)
- Pregnant women second-third trimester (≥16 weeks and <37 weeks) with *P. falciparum* infection (recruited at ANC visit)
- Active follow up of 63 days;
- Beyond 63 days: outcome of pregnancy and visit 3-6 weeks post partum
- Visit infant at 1st birthday;

Sites

malaria in pregnancy consortium

Baseline Results

- 3428 pregnant women with malaria were recruited to receive one of 4 ACT treatments (AL, AQAS (amodiaquine-artesunate), MQAS (mefloquine-artesunat) or DHAPQ)
- Burkina Faso 870, Ghana 788, Malawi 870, Zambia 900.
- 38% were symptomatic
- 23 years was the average age
- 23% ITN used before study entry
- 13 had IPT use before study entry

Treatment Outcomes by Country

Variable	AL	AQAS	MQAS	DHAPQ
Treatment success Rates (%)				
Ghana		99.5	100	99.5
Burkina Faso	93.2	96.7		92.5
Malawi	95.9	99.6	98.8	
Zambia	95.3		99.2	98.7
New Infections	34.4	11.9	17.0	8.3

- Higher new infections in AL

Early clearance

- At day 2 >99.5% parasite free
- Day 1 slide positivity
  - AL: 24.8%
  - AQAS: 6.9%
  - DHA-PQ: 8.0%
  - MQAS: 13.5%

P<0.001

Safety

% of patients

	AL (N=881)	ASAQ (N=842)	DHA-PQ (N=855)	MQAS (N=850)
SAE	0.7	2.6	2.2	2.9
AE	72.8	79.0	70.4	84.9
AE during first 7 days	24.3	59.5	34.2	60.7
Drug-Related AE	11.5	48.5	20.6	50.6
Drug-Related AE(occurring in >5% of patients in any treatment arm)				
Abdominal Pain	2.7	7.1	2.1	5.3
Asthenia	1.8	26.6	6.8	14.2
Decreased Appetite	0.3	8.2	2.1	7.7
Dizziness	1.2	23.5	1.6	30.6
Musculoskeletal Pain	0.8	7.2	2.6	4.4
Nausea	0.9	11.5	4.0	13.9
Vomiting	0.9	15.9	5.7	18.9

Safety

- Generally all treatments were well tolerated
- AL was associated with the fewest adverse events
- MQAS was associated with dizziness
- No difference in birth outcomes between the treaments

Pregnancy Outcome

	AL	ASAQ	DHA-PQ	MQAS
Miscarriages	1 (0.1)	4 (0.5)	4 (0.5)	4 (0.5)
Stillbirths	16 (1.9)	17 (2.1)	22 (2.7)	23 (2.8)
Preterm (echography)	174 (20.3)	144 (17.7)	179 (21.9)	127 (15.5)
Preterm (Ballard)	87 (10.2)	28 (3.4)	78 (9.5)	63 (7.7)
LBW	135 (17.2)	111 (15.5)	98 (14.1)	108 (15.2)
Mean BW (gr)	2,854	2,880	2,901	2,875
Congenital malformations	17 (2.0)	8 (1.0)	6 (0.8)	13 (1.7)

Conclusion

- AL had the best tolerability profile but the lowest efficacy and the shorter post-treatment prophylactic period.
- Higher occurrence of AEs in both the AQAS and MQAS groups
- Pregnancy outcomes and incidence of placental malaria were similar in all treatment arms
- DHA-PQ seems the most suitable treatment for uncomplicated malaria in pregnancy (good tolerability, high efficacy and long post-treatment prophylactic period);
- ASAQ and possibly MQAS (not as well tolerated but highly effective) may be good options for women with treatment failure after AL or DHA-PQ

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