

# ATAQ EASY

**Coarsucam<sup>®</sup> versus Coartem<sup>®</sup> for uncomplicated  
*Plasmodium falciparum* malaria**

**A multinational, randomized study comparing the  
tolerability and efficacy**

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# ATAQ EASY: Investigators

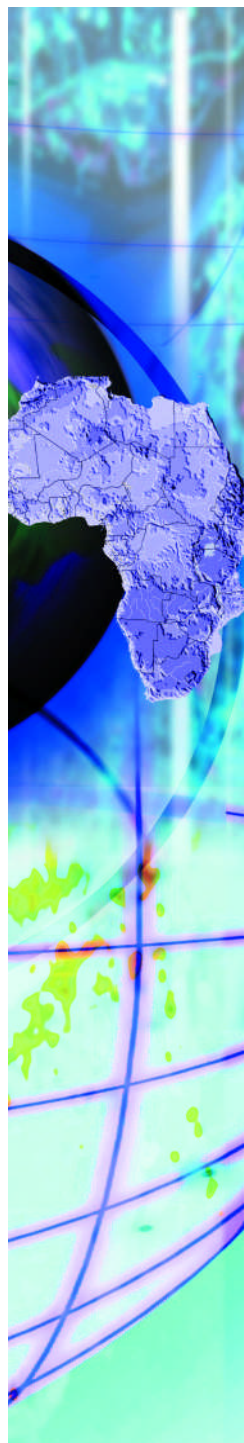
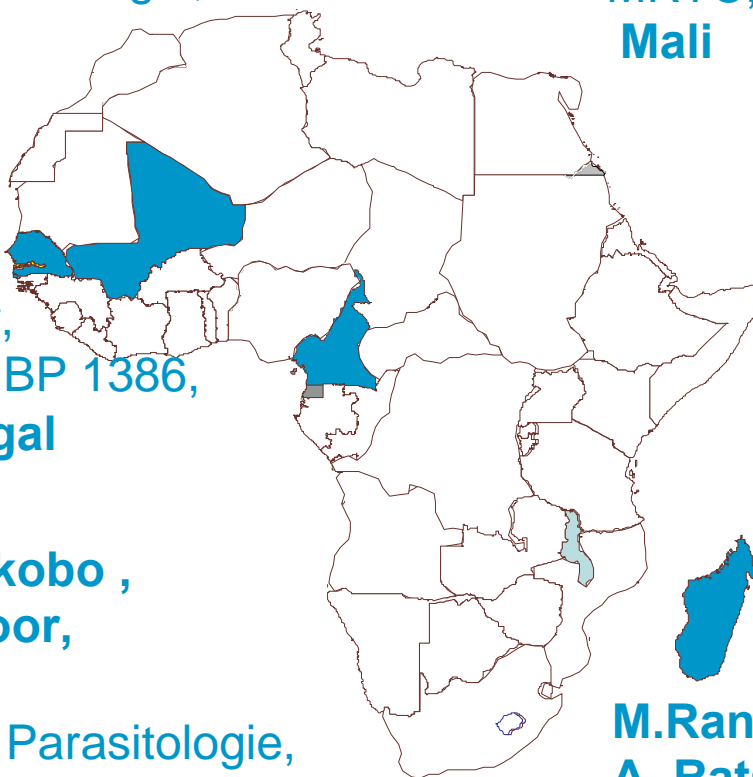
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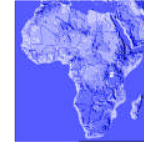
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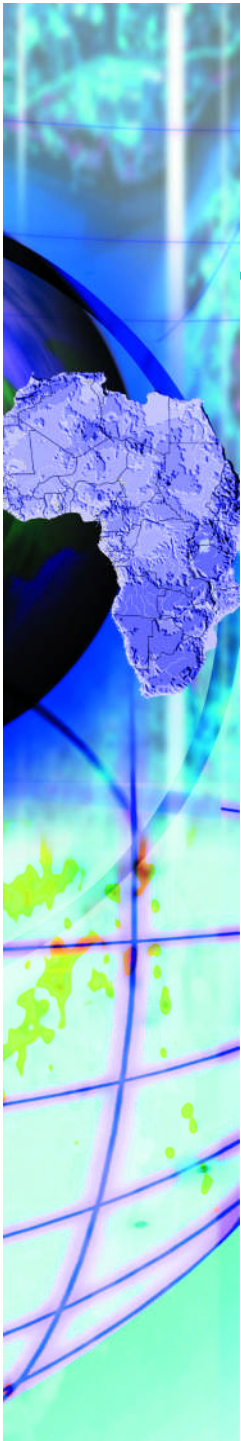


# ATAQ EASY: methods

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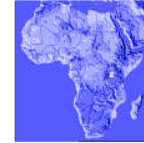


- Multicentre, Blinded, Randomized study (Mar-Dec 2006)
- 3 arms
  - Coarsucam<sup>®</sup> 1 intake a day (+ placebo)
  - Coarsucam<sup>®</sup> 2 intakes a day
  - Coartem<sup>®</sup> 2 intakes a day
- Adults and children over 10 kg with uncomplicated *P.falciparum* malaria attack (parasitemia  $\geq 1000/\mu\text{l}$ )
- Dosage according to bodyweight range



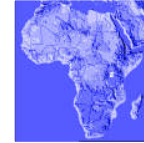
# ATAQ EASY: Objectives

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- **Primary objective** : to demonstrate the non inferiority of Coarsucam<sup>®</sup> one daily dose versus Coartem<sup>®</sup>, according to WHO 2003.
  - Acceptance limit for non inferiority was defined as 5 %.
- **Secondary objectives** :to compare the three treatment groups in terms of
  - efficacy as per WHO 2003,
  - Parasitological and fever clearances,
  - clinical and biological tolerability.

# ATAQ EASY: Analysis dataset



Included: n= 941

**Safety population: n=940**

Coarsucam<sup>®</sup> 1: n=313

Coarsucam<sup>®</sup> 2: n=315

Coartem<sup>®</sup> : n=312

n=1 : no treatment received

**ITT population: n=936**

Coarsucam<sup>®</sup> 1: n=310

Coarsucam<sup>®</sup> 2: n=315

Coartem<sup>®</sup> : n=311

n=4: double rejection of the first dose

**PP population: n=857**

Coarsucam<sup>®</sup> 1: n= 283

Coarsucam<sup>®</sup> 2:n=285

Coartem<sup>®</sup> : n=289

**n=79: major violations**

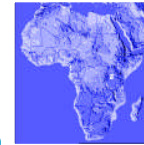
Dosage inadequate to bodyweight: n=5

Treatment duration < 3 days: n=3

Delay between morning and evening intake < 7h: n=39

No evaluation of primary criteria: n=32

# ATAQ EASY: Baseline characteristics



	Coarsucam® 1 intake n=313	Coarsucam® 2 intakes n=315	Coartem® 2 intakes n=312
<b>Gender n (%)</b>			
Female	137 (43.8%)	145 (46.0%)	145 (46.5%)
Male	176 (56.2%)	170 (54.0%)	167 (53.5%)
<b>Age (years) n (%)</b>			
< 5 years	146 (46.6%)	148 (47.0%)	142 (45.5%)
>= 5 years	167 (53.4%)	167 (53.0%)	170 (54.5%)
<b>Temperature (°C) Mean (SD)</b>	37.937 (1.087)	38.043 (1.043)	37.919 (1.066)
<b>Parasitic density /μL Mean (SD)</b>	313 (0) 37780.87 (45651.62)	315 (0) 41862.97 (49049.13)	312 (0) 33958.29 (41473.55)

•Patient baseline characteristics were comparable between groups.

# ATAQ EASY: Efficacy Results

## Primary endpoint (1)



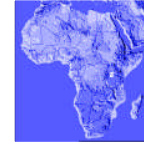
PCR corrected D28 cure rate (ITT population)	Coarsucam® 1 intake n=310	Coartem® 2 intakes n=311
Possible failure	12 (3.9%)	9 (2.9%)
ETF	0	0
LCF	0	2 (0.6%)
LPF	3 (1.0%)	3 (1.0%)
<b>ACPR</b>	<b>295 (95.2%)</b>	<b>297 (95.5%)</b>

**NON INFERIORITY DEMONSTRATED**

The two-sided 90% CI of the difference in the proportions of ACPR is : [-0.03 ; **0.03**]  
Upper limit of CI < 0.05 ( non-inferiority delta)

# ATAQ EASY: Efficacy Results

## Primary endpoint (2)



PCR corrected D28 cure rate (PP population)	Coarsucam® 1 intake n=283	Coartem® 2 intakes n=289
ETF	0	0
LCF	0	1 (0.3%)
LPF	3 (1.1%)	3 (1.0%)
<b>ACPR</b>	<b>280 (98.9%)</b>	<b>285 (98.6%)</b>

### NON INFERIORITY DEMONSTRATED

The two-sided 90% CI of the difference in the proportions of ACPR is : [-0.02 ; **0.01**].  
Upper limit of CI < 0.05 ( non-inferiority delta)



# ATAQ EASY: Efficacy Results

## Secondary endpoints



IC [-0.03 ; 0.03]

IC [-0.02 ; 0.04]

PCR corrected D28 cure rate (ITT population)	Coarsucam® 1 intake n=310	Coarsucam® 2 intakes n=315	Coartem® 2 intakes n=311
Possible failure	12 (3.9%)	16 (5.1%)	9 (2.9%)
ETF	0	0	0
LCF (Late clinical failure)	0	0	2 (0.6%)
LPF (Late parasitological failure)	3 (1.0%)	0	3 (1.0%)
<b>ACPR</b>	<b>295 (95.2%)</b>	<b>299 (94.9%)</b>	<b>297 (95.5%)</b>

IC [-0.03 ; 0.00]

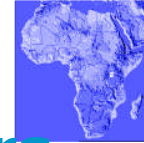
IC [-0.03 ; 0.00]

PCR corrected D28 cure rate (PP population)	Coarsucam® 1 intake n=283	Coarsucam® 2 intakes n=285	Coartem® 2 intakes n=289
ETF	0	0	0
LCF	0	0	1 (0.3%)
LPF	3 (1.1%)	0	3 (1.0%)
<b>ACPR</b>	<b>280 (98.9%)</b>	<b>285 (100.0%)</b>	<b>285 (98.6%)</b>

**NON INFERIORITY DEMONSTRATED**

# ATAQ EASY: Efficacy Results

## Secondary endpoints: children < 5 years



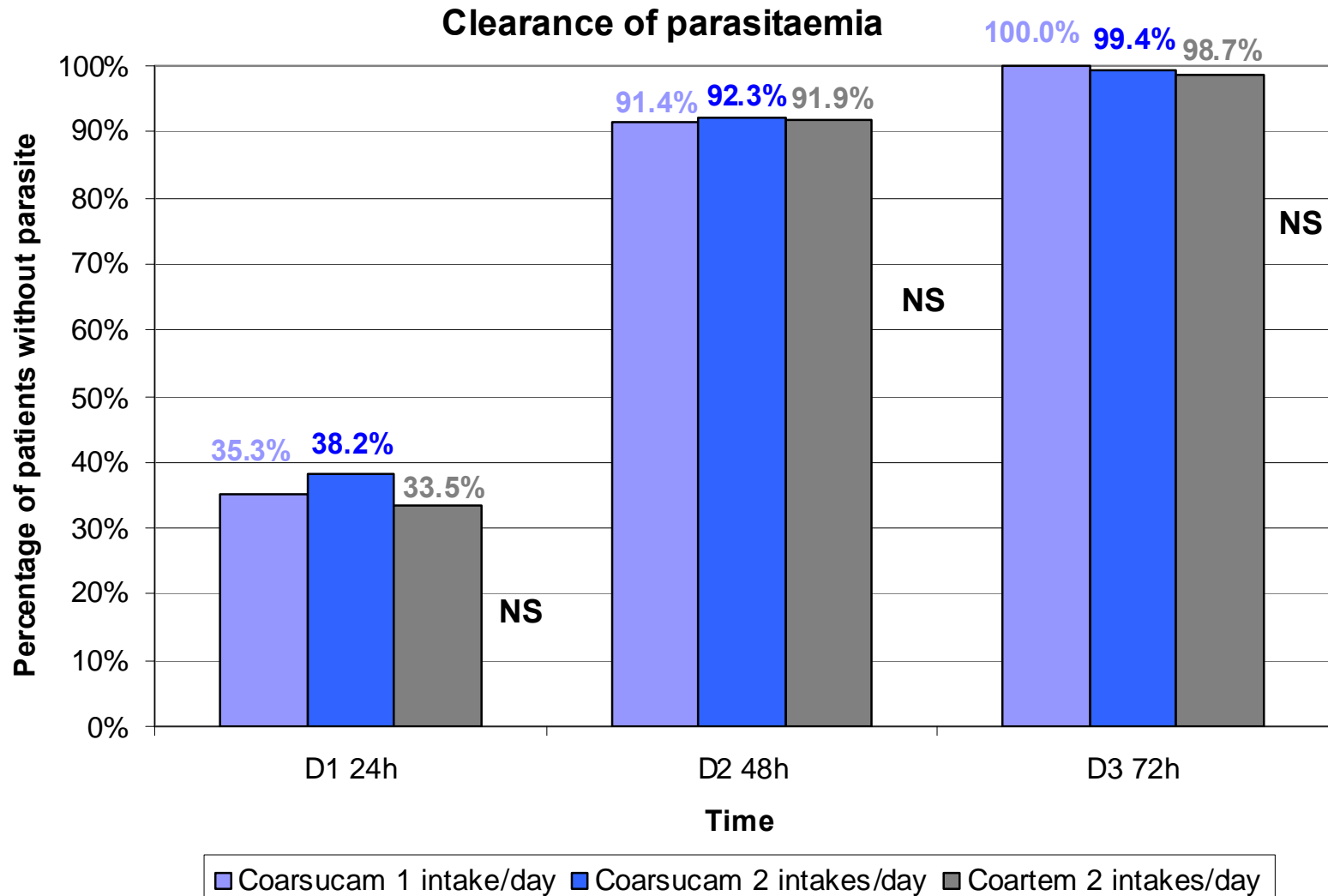
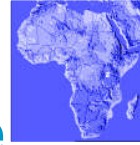
IC: [-0.06 ; 0.04]).

Efficacy evaluation on D28 after PCR correction on the ITT population (subgroup : age)	Coarsucam® 1 intake n=143	Coarsucam® 2 intakes n=148	Coartem® 2 intakes n=142	Total n=433
Age < 5 years				
Possible failure	6 (4.2%)	6 (4.1%)	4 (2.8%)	16 (3.7%)
ETF	0	0	0	0
LCF	0	0	2 (1.4%)	2 (0.5%)
LPF	2 (1.4%)	0	3 (2.1%)	5 (1.2%)
<b>ACPR</b>	<b>135 (94.4%)</b>	<b>142 (95.9%)</b>	<b>133 (93.7%)</b>	<b>410 (94.7%)</b>

**NON INFERIORITY DEMONSTRATED**

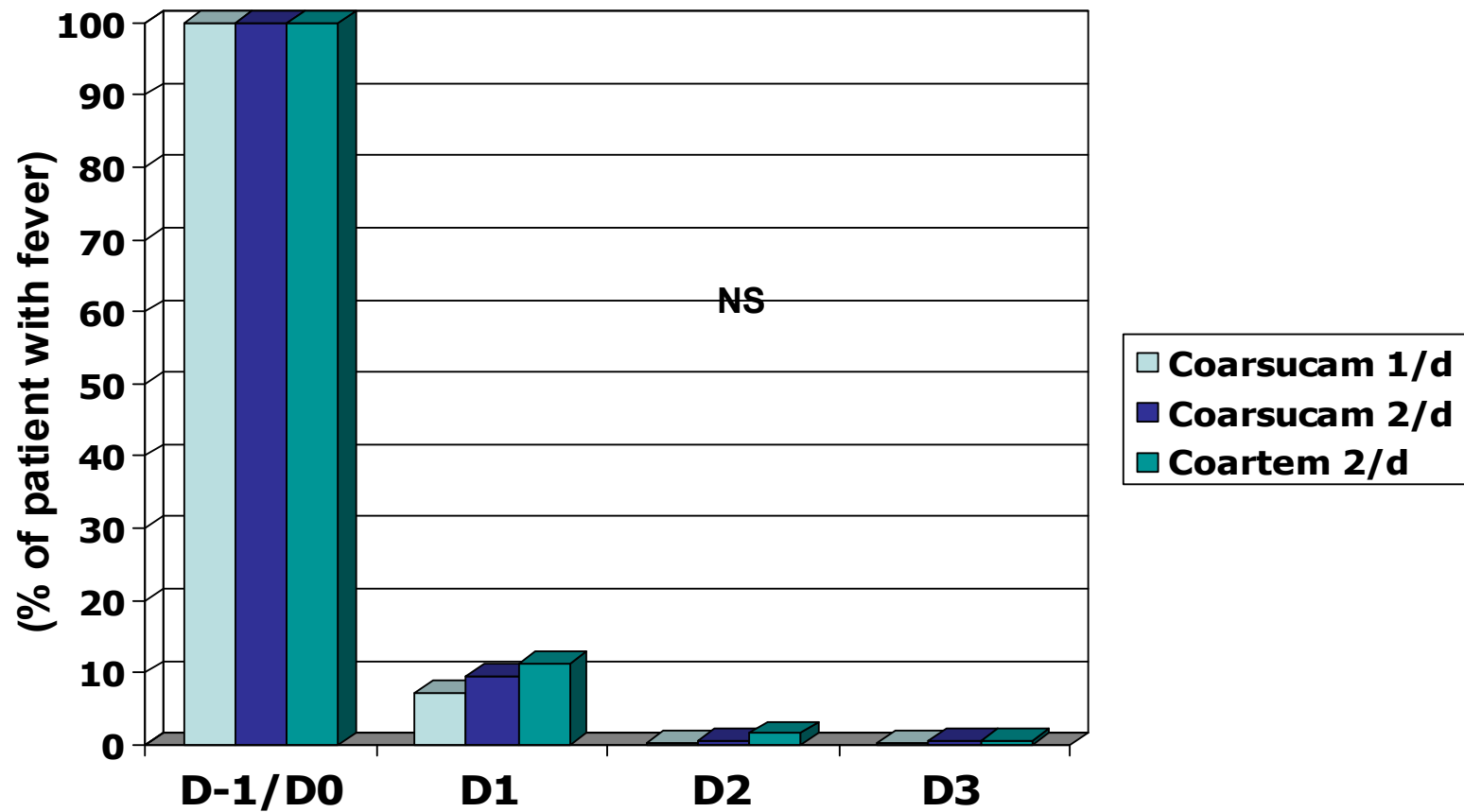
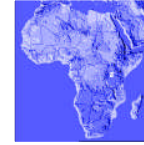
# ATAQ EASY: Efficacy Results

## Secondary endpoints : parasitological clearance

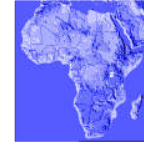


# ATAQ EASY: Efficacy Results

Secondary endpoints: Fever resolution



# ATAQ EASY: Safety Results



- Withdrawals due to treatment intolerance n=8 (0.9%)

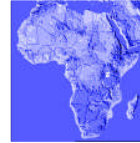
	<b>Coarsucam® 1 intake n=313</b>	<b>Coarsucam® 2 intakes n=315</b>	<b>Coartem® 2 intakes n=312</b>
Adverse event leading to treatment discontinuation	3* (1.0%)	0	0
Double rejection on D0	4 (1.3%)	0	1 (0.3%)

\*Dizziness,asthenia, vomiting

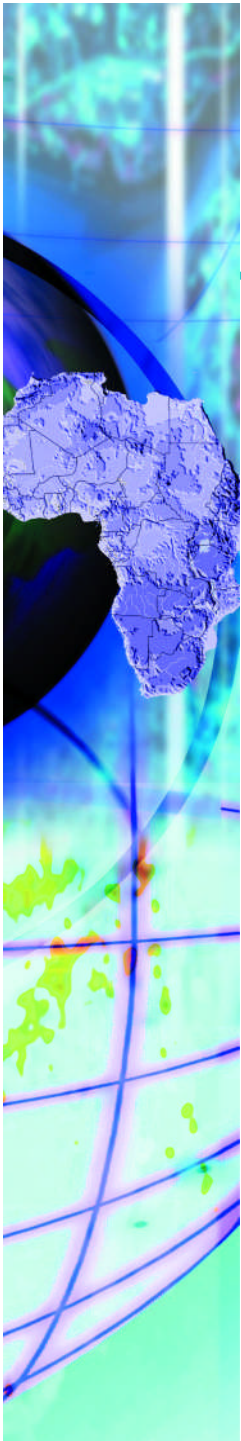
# ATAQ EASY: Safety Results

## **Serious adverse events**

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- Coarsucam<sup>®</sup> 1/day, n=2 :
  - Anemia+lung infection (death)
  - Anemia (full recovery after hospitalization)
- Coartem<sup>®</sup> 2/day, n=1
  - Coma (death)

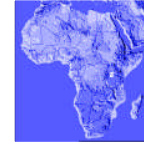




# ATAQ EASY: Safety Results

<b>Emergent adverse events</b>	<b>Coarsucam™ 1 intake ( 145 AE in 105 patients)</b>	<b>Coarsucam™ 2 intake ( 116 EA in 85 patients)</b>	<b>Coartem® ( 122 AE in 85 patients)</b>
<b>Blood And Lymphatic System Disorders</b>	5 ( anemia)	2 ( anemia)	1 ( anemia)
<b>Cardiac Disorders</b>	2 ( arrhythmia)	2 ( arrhythmia, bradycardia)	1( palpitations)
<b>Ear and Labyrinth disorder</b>	1( vertigo)		1( tinnitus)
<b>Eyes disorder</b>	3 ( conjunctivitis)		2 ( conjunctivitis)
<b>Gastrointestinal Disorders</b>	22 ( abdominal pain, diarrhoea, nausea, vomiting)	20 ( diarrhoea, nausea, pain,constipation, vomiting)	9 ( abdominal pain, diarrhoea, nausea, stomatis,vomiting)
<b>General Disorders And Administration Site Conditions</b>	5 ( face oedema,localised oedema, asthenia, pyrexia)	4 ( malaise, pain, face oedema)	6 ( face oedema, peripheral oedema,local oedema,pyrexia asthenia)
<b>Infections And Infestations</b>	67	54	63
<b>Injury,Poisoning and procedural complications</b>	2	5	4
<b>Metabolism And Nutrition Disorders</b>	2 ( hypoglycemia, malnutrition)		
<b>Musculoskeletal And Connective Tissue Disorders</b>	1( arthralgia)		1 ( myalgia)
<b>Nervous System Disorders</b>	11 ( somnolence)	3 ( somnolence, paresthesia, headache)	4 ( headache, coma,convulsion)
<b>Psychiatric Disorders</b>	3 ( insomnia, hallucination)	4 ( hallucination, insomnia)	1( insomnia)
<b>Renal and urinary disorders</b>			1 (haematuria)
<b>Respiratory, Thoracic And Mediastinal Disorders</b>	18 ( cough)	15 ( cough, rhinitis,epistaxis)	11 ( cough, epistaxis)
<b>Skin And Subcutaneous Tissue Disorders</b>	3( pruritus, rash)	1 (rash pruritic)	5( rash, pruritus,toxic epidermal necrolysis)
<b>Vascular Disorders</b>	1 ( hypertension)		2( pallor)

# ATAQ EASY: Safety Results



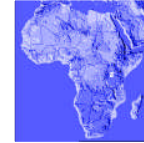
- Rejection or vomiting in the half hour past treatment administration between D0 and D2

Vomiting or Rejection	Coarsucam® 1 intake n=313	Coarsucam® 2 intakes n=315	Coartem® 2 intakes n=312	Total n=940
<b>&lt; 5 years –</b>				
no	146	148	142	436
Yes	30 (20.5%)	30 (20.3%)	22 (15.5%)	82 (18.8%)
<b>[5; 14[ years –</b>				
no	105	113	112	330
Yes	10 (9.5%)	15 (13.3%)	10 (8.9%)	35 (10.6%)
<b>≥ 14 years –</b>				
no	62	54	58	174
Yes	2 (3.2%)	2 (3.7%)	1 (1.7%)	5 (2.9%)
<b>P-value (Khi<sup>2</sup> test)</b>	<b>0.0013</b>	<b>0.0115</b>	<b>0.0126</b>	<b>&lt; 0.0001</b>

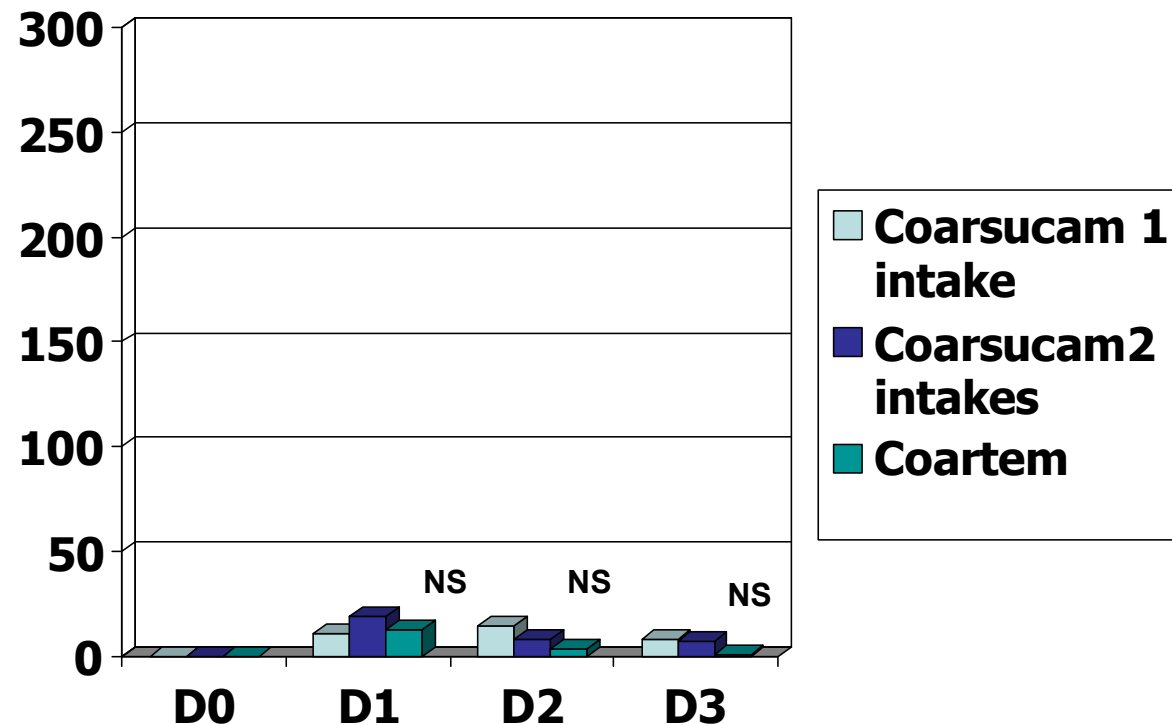
- Significant statistical differences between age ranges
- No significant difference among treatment groups



# ATAQ EASY: Safety Results

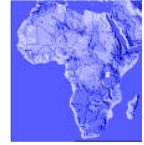


- Incidence of vomiting after D0



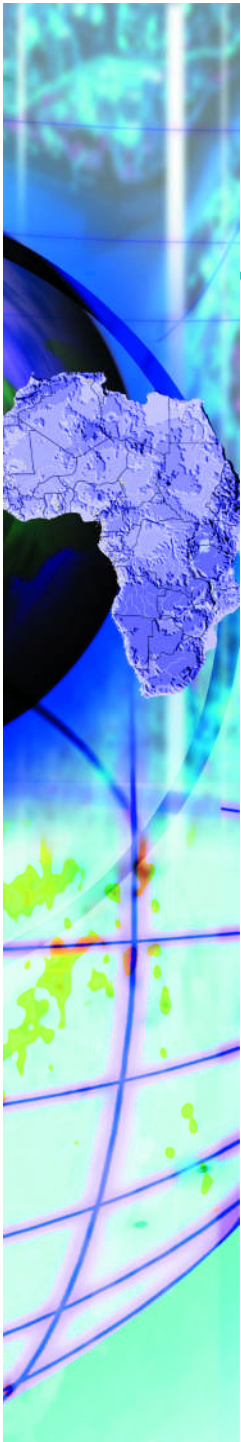
**No significant difference among treatment groups**

# ATAQ EASY: Biological Results



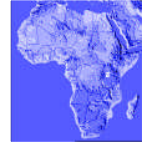
**No significant difference among treatment groups**

- Haematology:
  - leucocytes, neutrophils, platelets, hemoglobin
- Biochemistry:
  - ALAT, ASAT, creatininemia



# ATAQ EASY: Conclusions

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- Non inferiority of Coarsucam<sup>®</sup> vs Coartem<sup>®</sup>, included in children under 5 years old, demonstrated
- Comparable level of clinical and biological safety in the 3 groups of treatment; no unexpected adverse event

