

# **Evaluation of 4 artemisinin-based combinations for treating uncomplicated malaria in African children**

## ***Preliminary results***

*Umberto D 'Alessandro and  
the 4ABC study group*

# Objectives



- **Main**

- To compare **the safety and efficacy of 4 ACT**, i.e. AQ+AS, AL, DHAPQ, CDA, for single and repeat treatments of uncomplicated malaria

- **Specific**

- To evaluate the efficacy of the 4 ACTs for the treatment of children with uncomplicated *P. falciparum* malaria (**first active follow-up**);
- To determine after the first active follow-up the **incidence rate of a second clinical episode** of uncomplicated *P. falciparum* malaria

- **Specific**
  - To evaluate the efficacy of treating the II clinical episode of uncomplicated *P. falciparum* malaria with the same ACT used for the first one (**second active follow-up**);
  - To evaluate **safety** of the 4 ACTs for the treatment of children with uncomplicated *P. falciparum* malaria;

# Study design



- 3-arm multicentre, randomised, open label;
- First follow up of 28 days;
- Beyond 28 days: Passive follow-up for detection of a second clinical episode within 6 months;-> re-treatment;
- Second follow-up of 28 days;
- 510 patients per site/ 170 per arm

# Study treatments by country



<i>Country</i>	<i>N. sites</i>	<i>Study treatments</i>		
Burkina Faso	1	AQ+AS	DHAPQ	AL
Nigeria	1	AQ+AS	DHAPQ	AL
Zambia	1	AQ+AS	DHAPQ	AL
Gabon	1	AQ+AS	DHAPQ	AL
Uganda	1	DHAPQ	CDA	AL
Uganda	2	AQ+AS	CDA	DHAPQ
Rwanda	2	DHAPQ	CDA	AL
Mozambique	1	AQ+AS	CDA	DHAPQ

# End points



- **Primary**
  - TF PCR adjusted and unadjusted up to day 28
- **Secondary**
  - TF up to day 63 (unadjusted and for the whole period of passive surveillance)
  - TF second clinical episode (D28 and D63);
  - Fever & parasite clearance time.
  - Gametocytaemia
  - Hb changes

# Inclusion criteria

- Age 6 months and 59 months inclusive
- Body weight  $\geq 5$  Kg
- Monoinfection of *Plasmodium falciparum* (parasitaemia  $\geq 1,000/\mu\text{L}$  to  $200,000/\mu\text{L}$ ).
- Fever/history of fever
- Haemoglobin value  $\geq 7.0$  g/dl
- Signed informed consent

# Exclusion criteria



- Participation in any investigational drug study during the previous 30 days.
- Known hypersensitivity to the study drugs.
- Severe malaria or danger signs
- Presence of intercurrent illness
- Severe malnutrition
- Ongoing prophylaxis with drugs having antimalarial activity

# Passive follow up



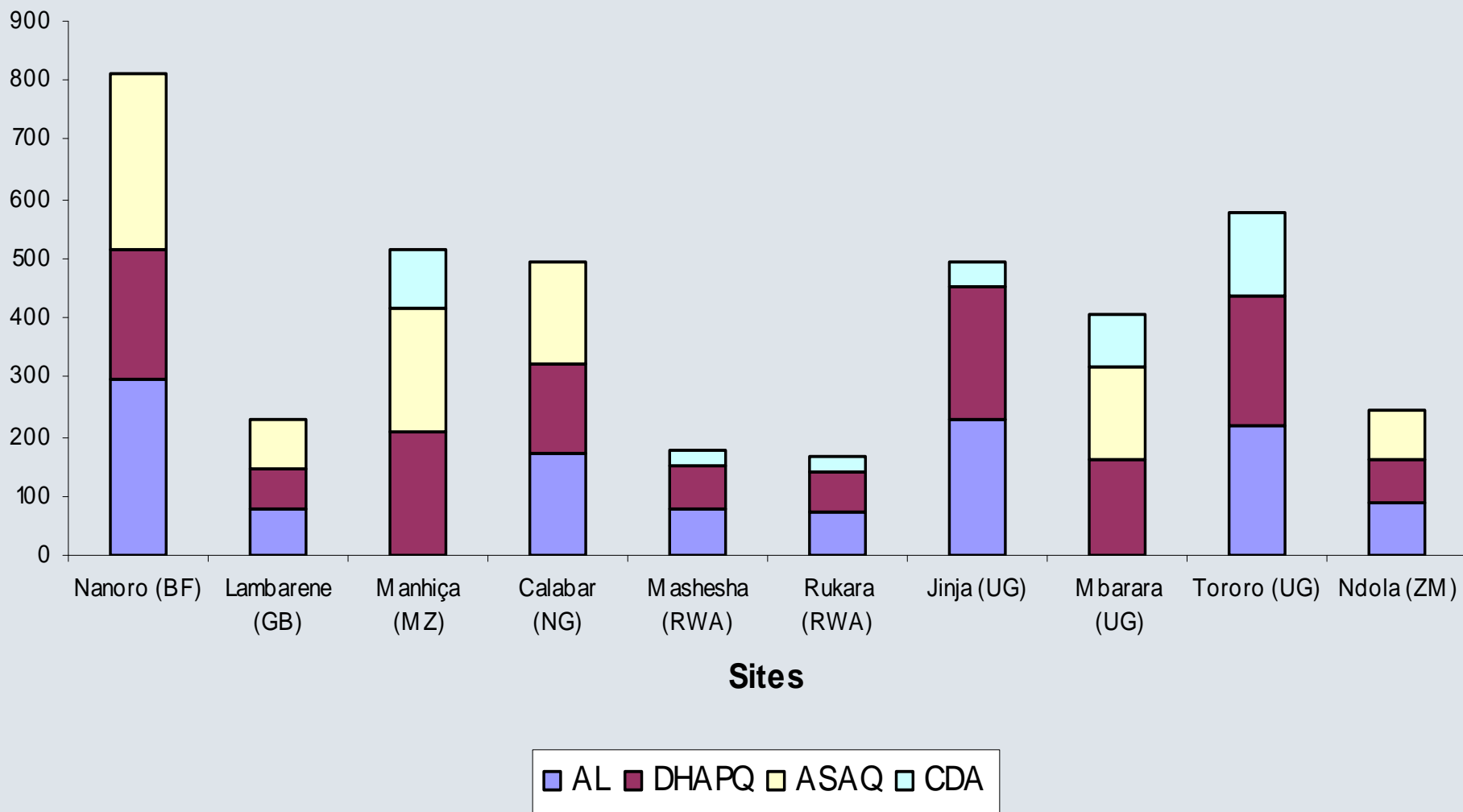
- Parents/guardians asked to attend for any illness;
- Monthly visits at home to keep contact without collecting blood samples unless sick;
- When attending HC, blood slides, BT and Hb/PCV collected systematically;
- If inclusion criteria included in the second follow up;
- If malaria not fulfilling criteria, treated with I line treatment;

# Amendements

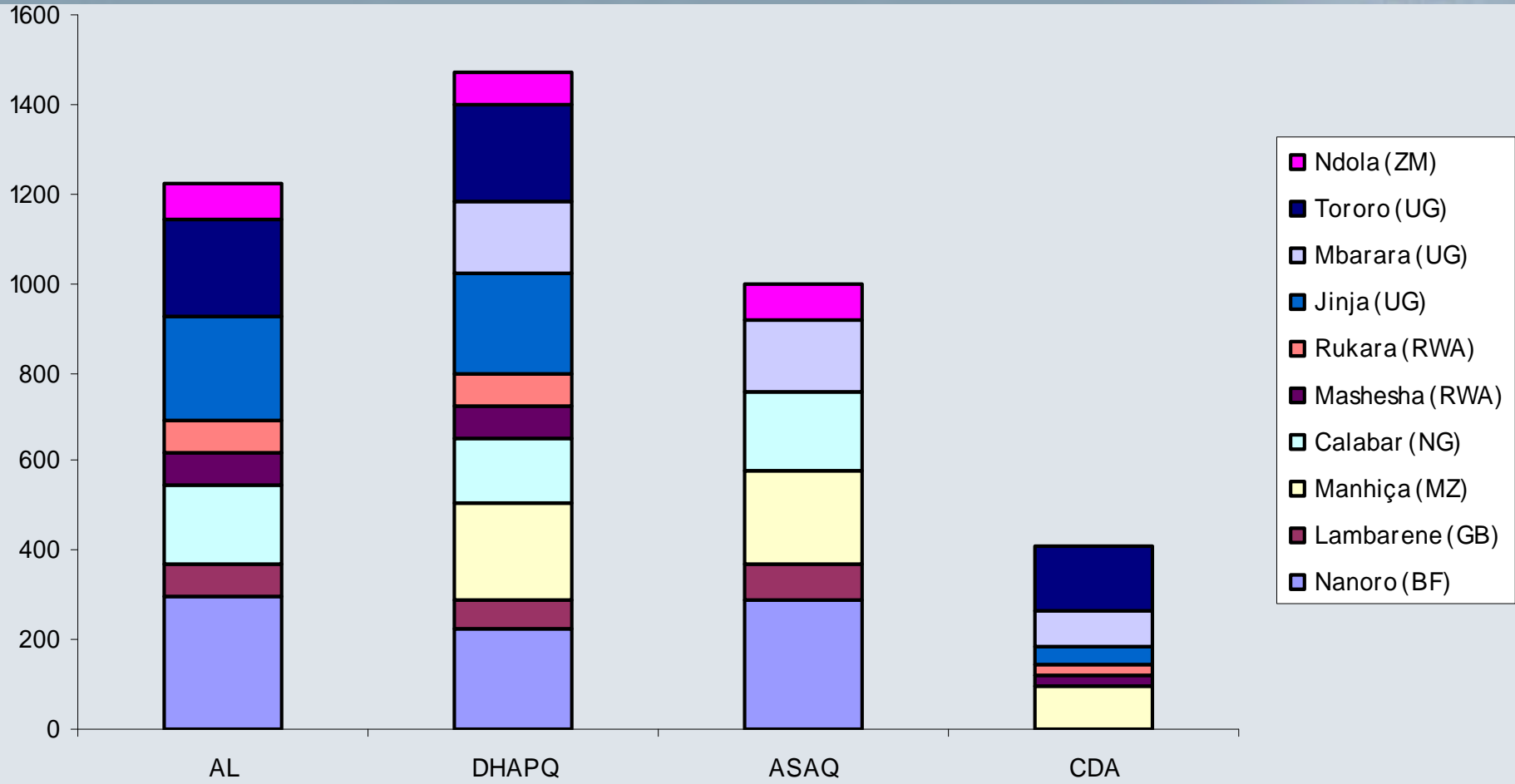


- First (February 2007)
  - Some adjustments to the protocol
- Second (February 2008)
  - Stop of the CDA arm
  - Re-distribution of patients between sites: ↑ patients in Nanoro (BF) and Tororo (Uganda)
- Third (October 2008)
  - Discontinuation of DHA-PQ arm as product not available

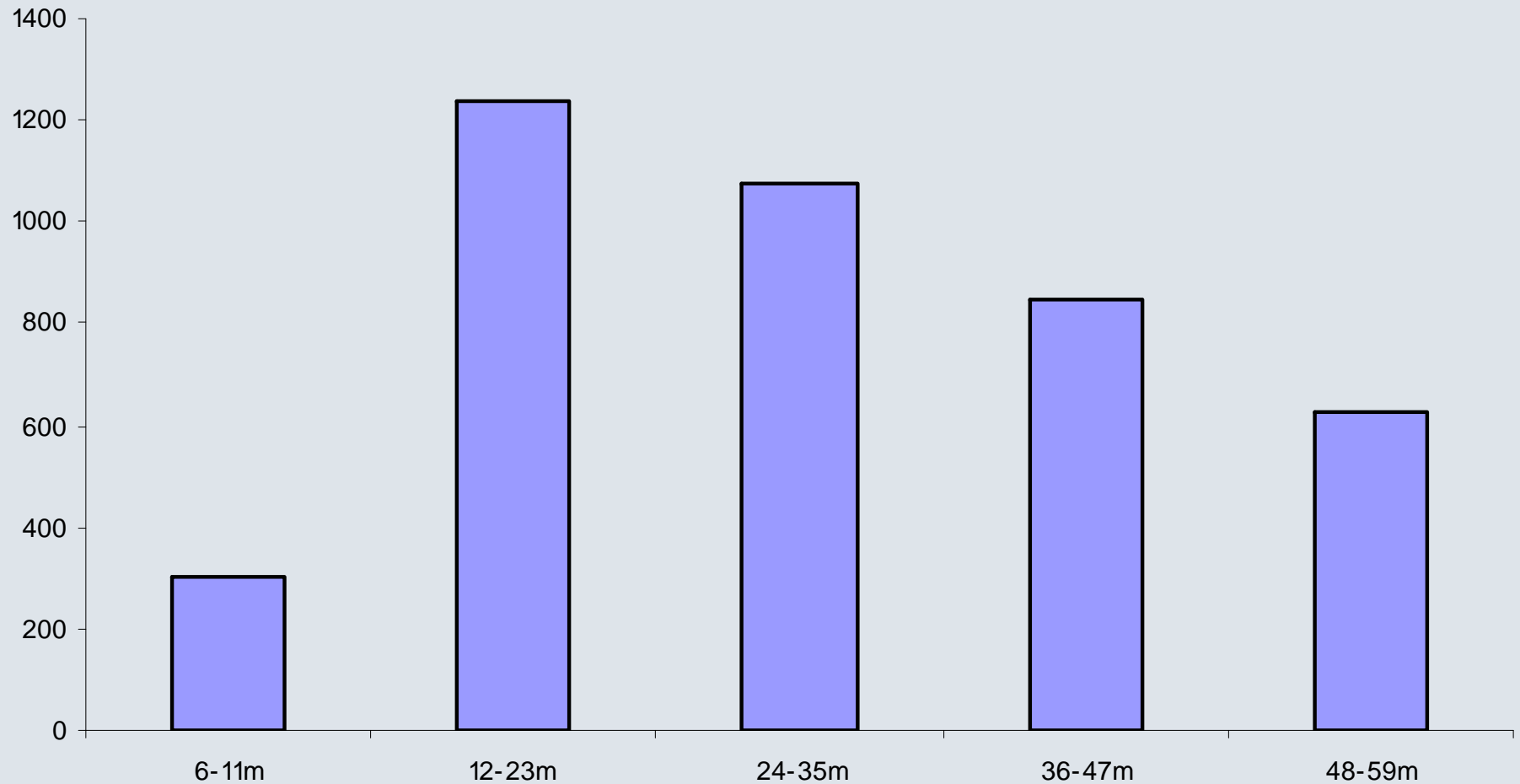
# Number of patients by site and treatment



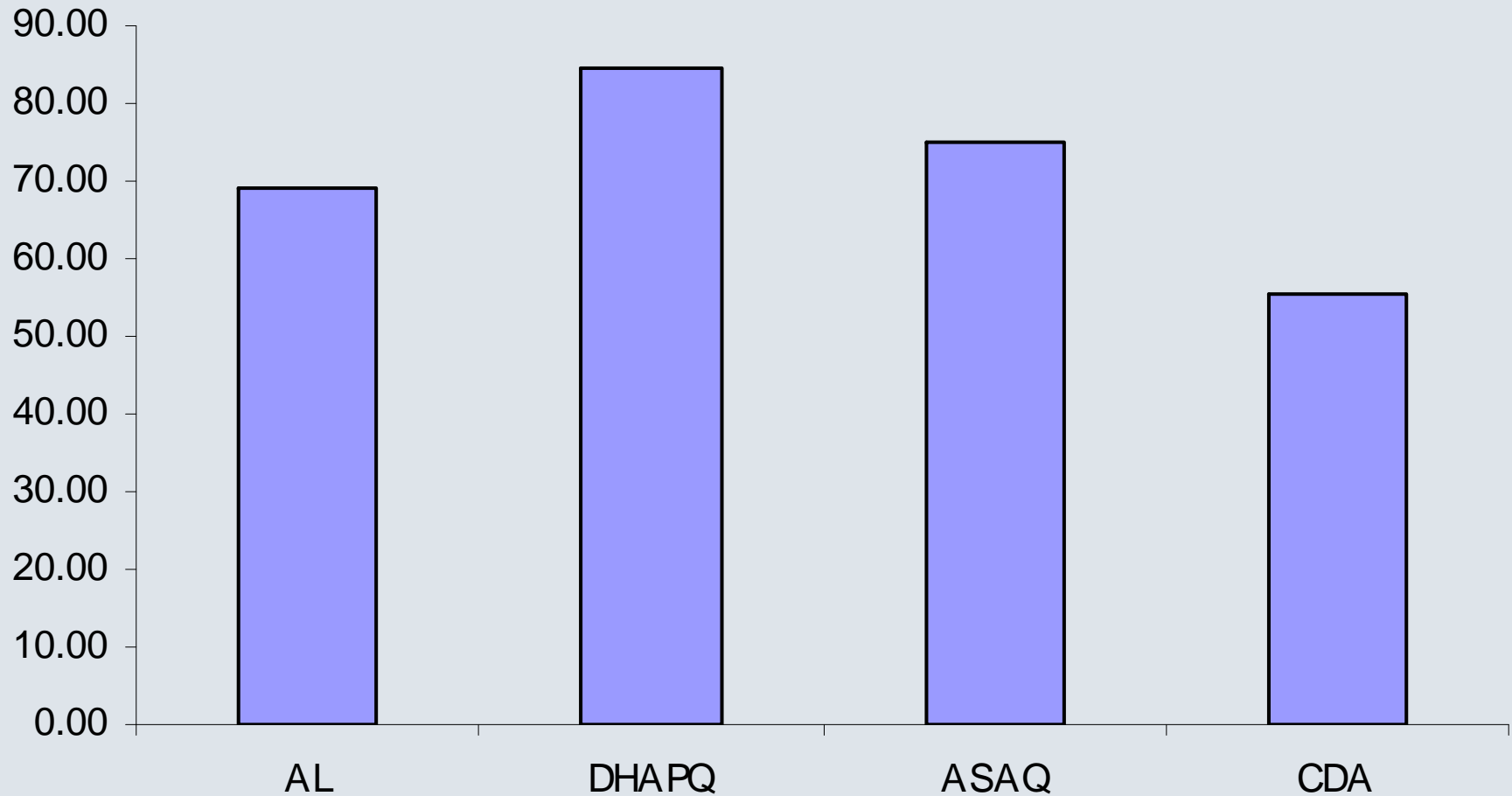
# Number of patients by treatment and site



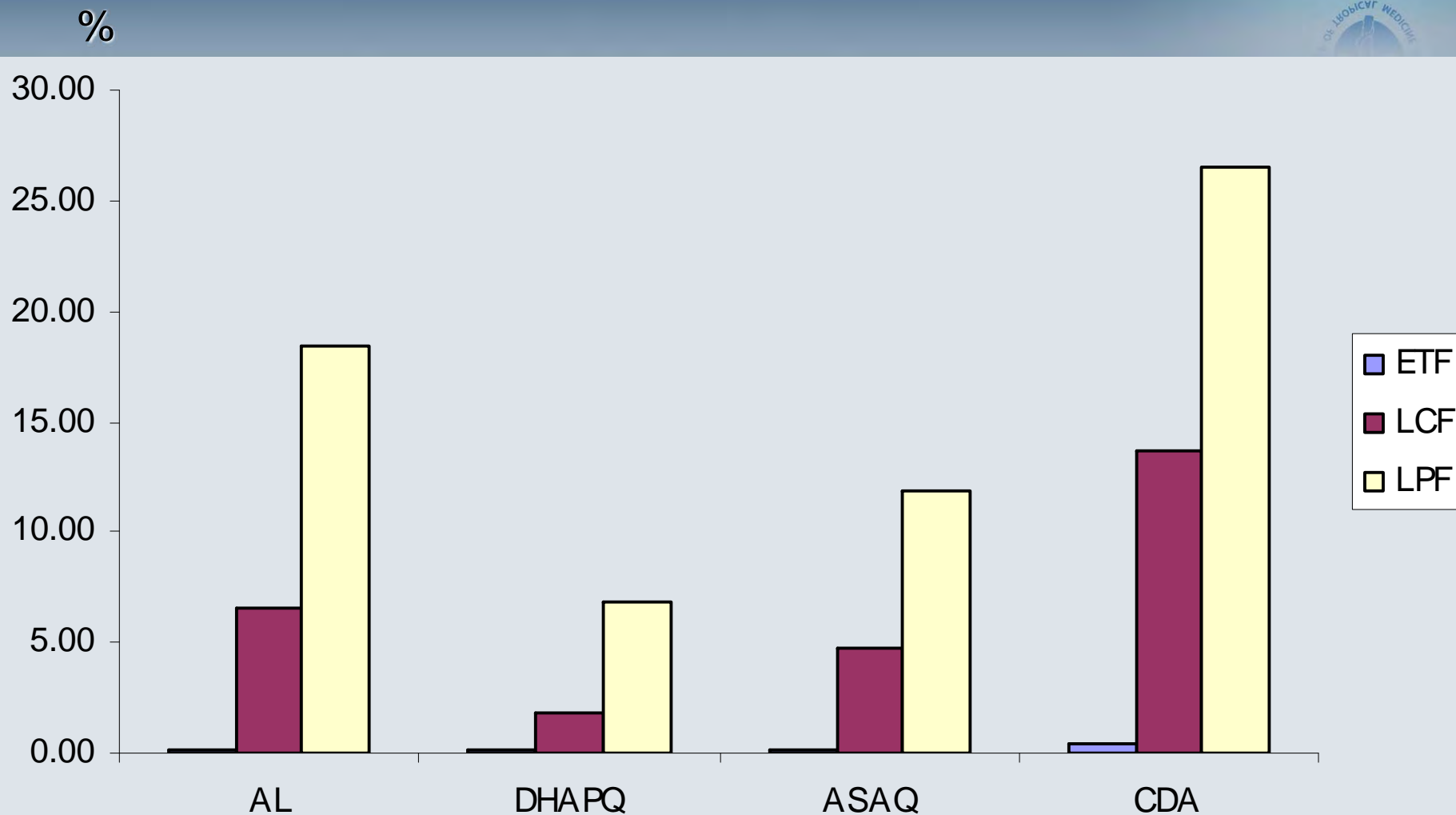
# Patients' age group distribution



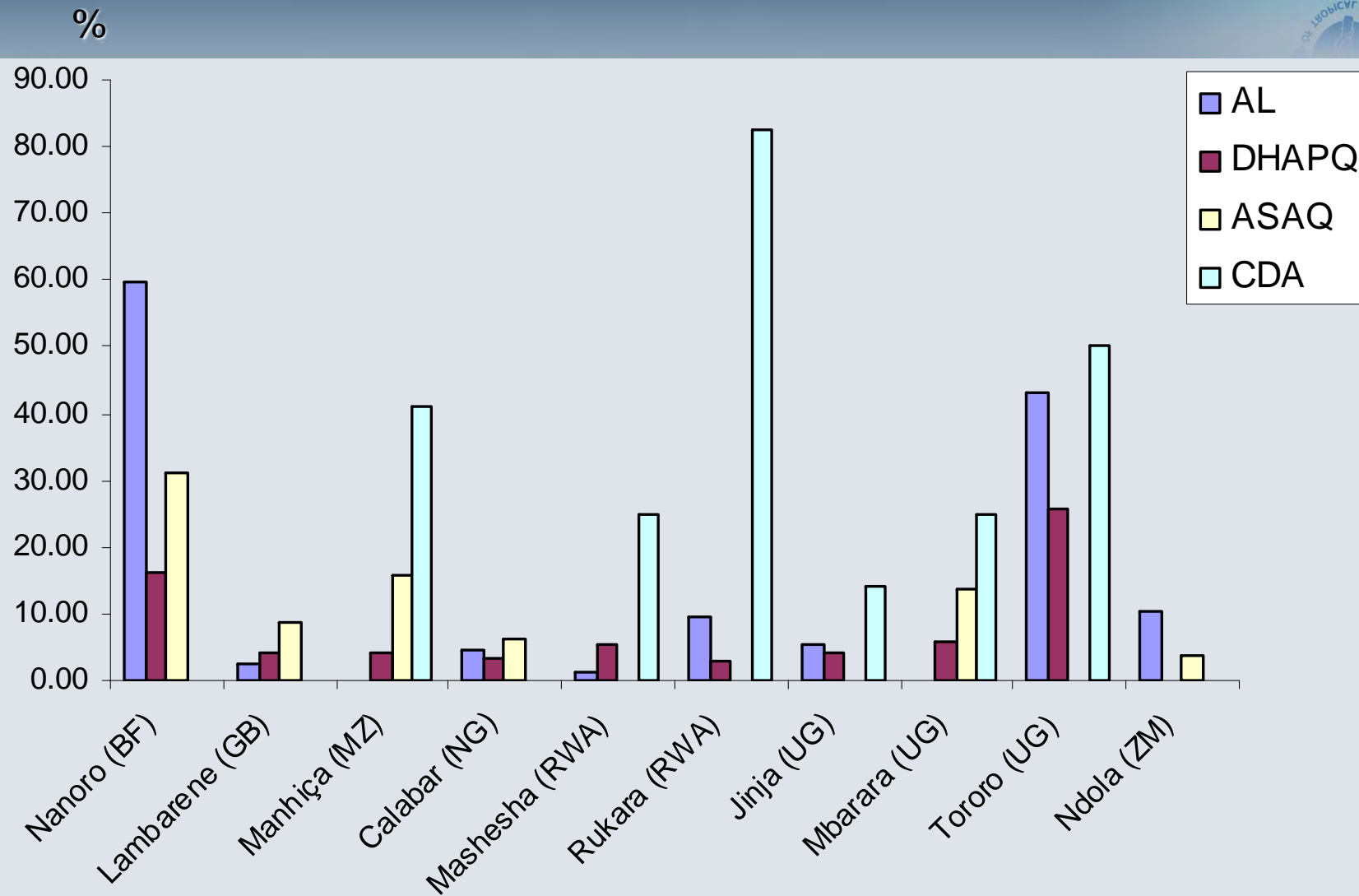
# ACPR D28 (uncorrected) by treatment



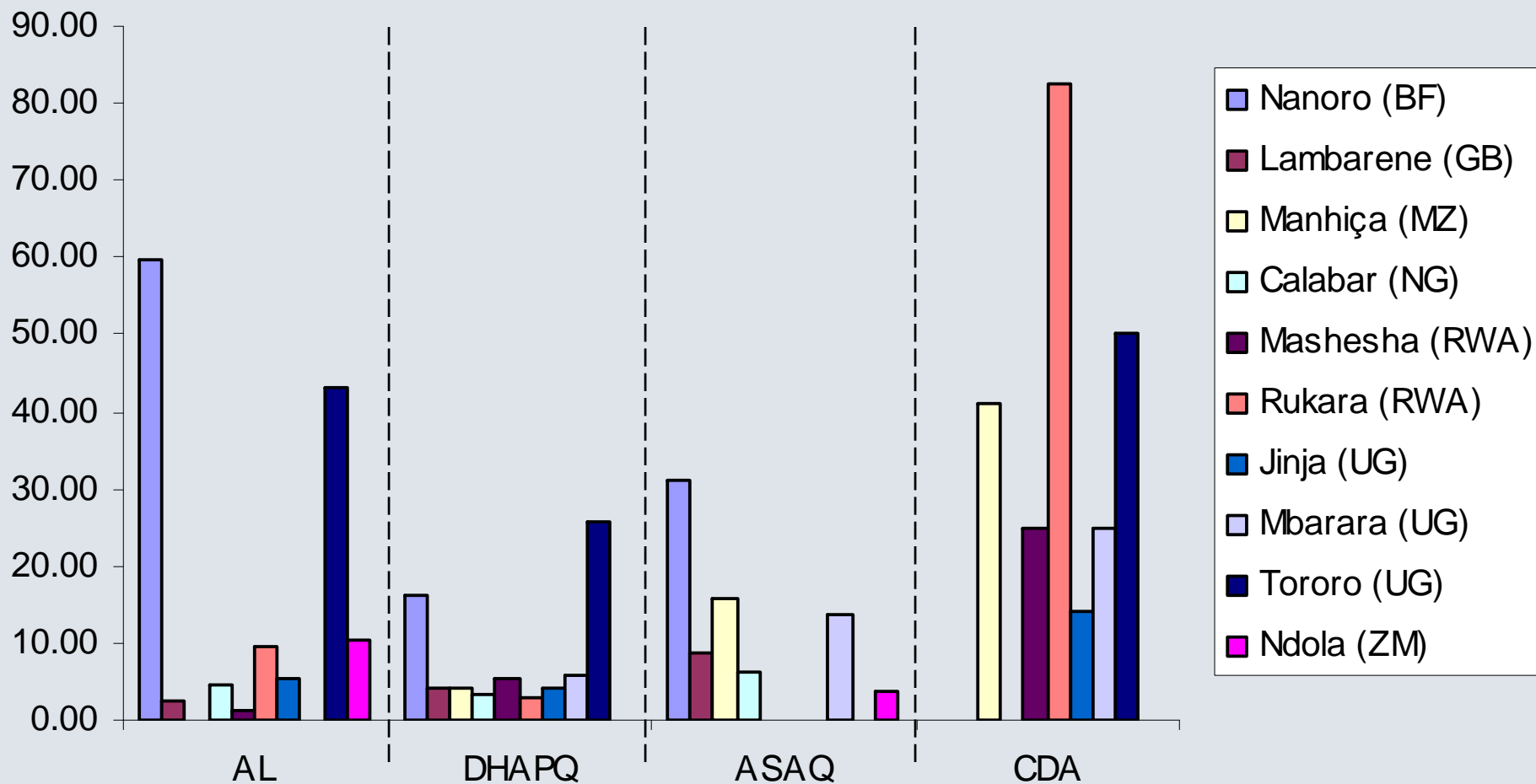
# Treatment failure D28 (uncorrected) by treatment



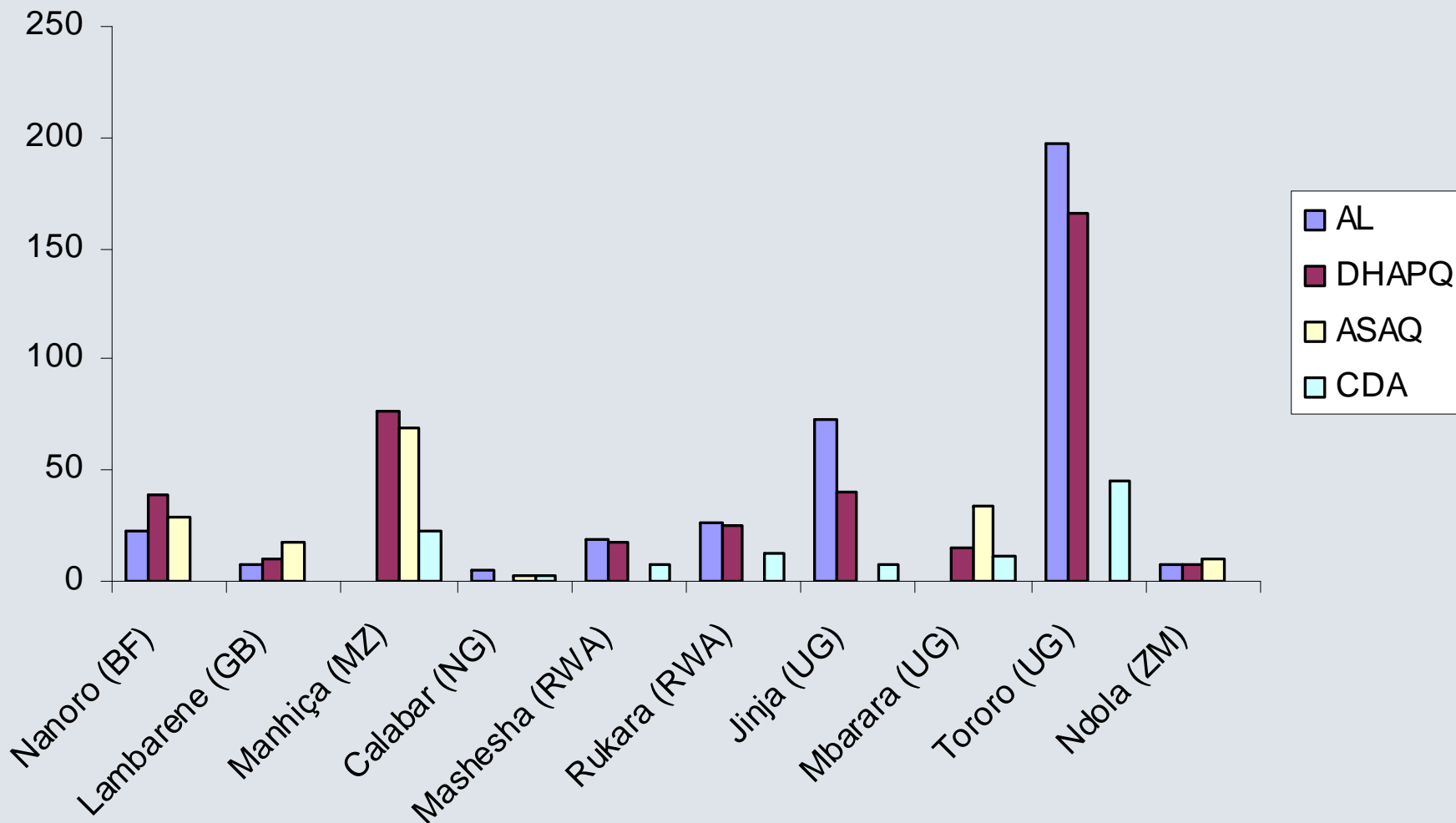
# Treatment failure D28 (uncorrected) by site



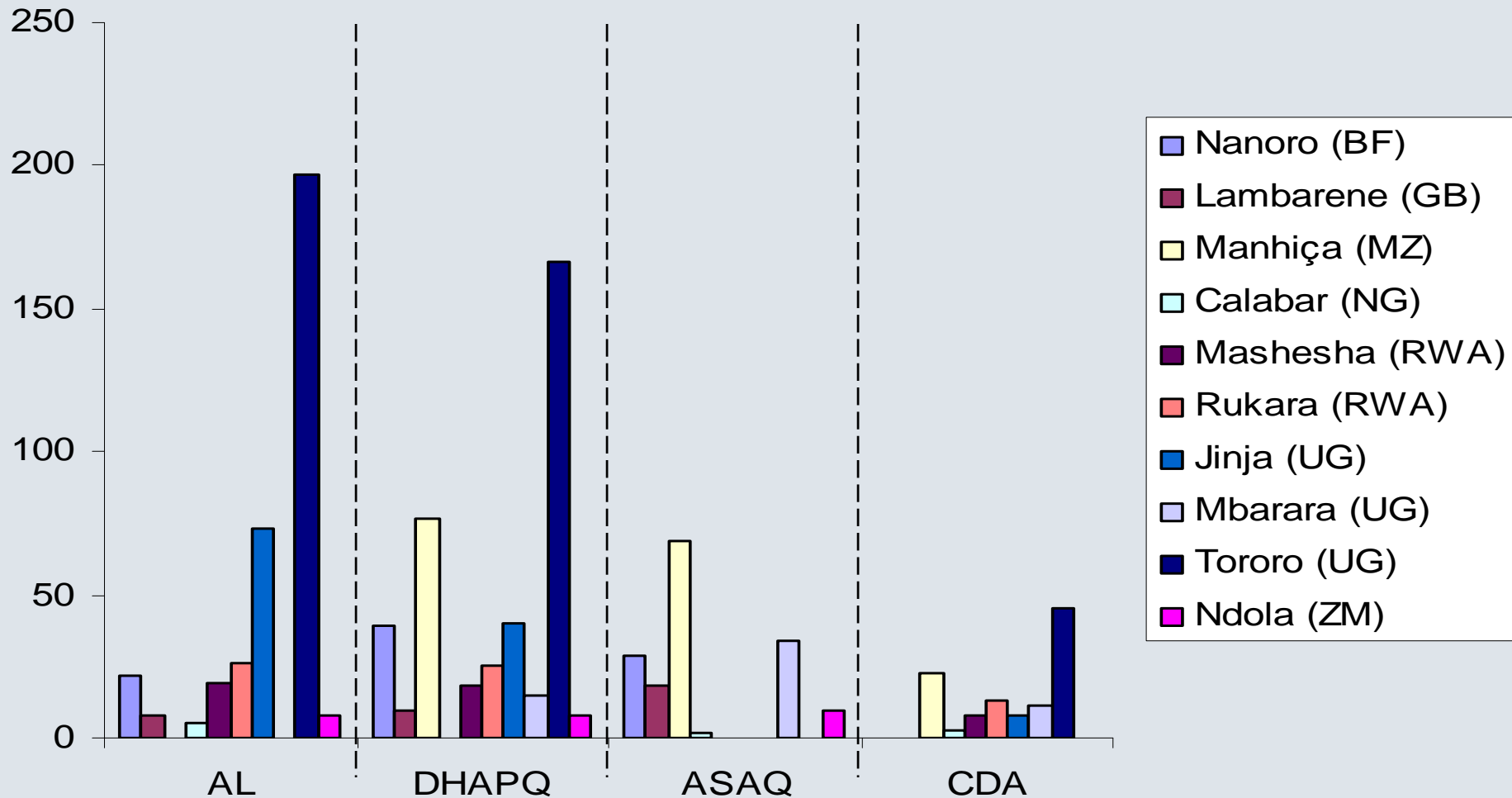
# Failure by treatment



# Number of patients in II active FU by site



# Number of patients in II active FU by treat



# SAE and deaths (13) by treatment



# Ongoing activities



- Genotyping: about 2000 samples to process
- Lock database by the end of December 2009
- Clinical study report by June 2010

# Institutions involved



- Institute of Tropical Medicine, Antwerp, Belgium
- Liverpool School of Tropical Medicine and Centre for Medical Statistics and Health Evaluation, University of Liverpool, UK
- East African Network for Monitoring Antimalarial Treatment (EANMAT).
- Centre Muraz, Bobo Dioulasso, Burkina Faso.
- Department of Paediatrics, University of Calabar, Cross River State, Nigeria.
- Tropical Diseases Research Centre, Ndola, Zambia
- Institute of Tropical Medicine, Department of Parasitology, University of Tuebingen, Germany and Medical Research Unit,
- Albert Schweitzer Hospital, Lambaréné, Gabon.
- Uganda Malaria Surveillance Project (UMSP), Kampala, Uganda.
- Epicentre, Paris, France and Mbarara University of Science and Technology, Faculty of Medicine, Mbarara, Uganda
- Programme National de Lutte contre le Paludisme, Kigali, Rwanda.
- Fundacio Clinic per a la Recerca Biomèdica/Centre for International Health, University of Barcelona, Spain and Manhica Health Research Center, Mozambique.