# UPE 166

Clinical Research Centre 13 ring road, x 10005 Kampala, Uganda vmusiime

#### C Clinical Trials Unit 2 Euston Road, London, NW1 2DA Tel: +44 20 7670 4894 Fax: +44 20 7670 4818

# Bacteraemia in HIV-1 infected children on antiretroviral therapy in Uganda and Zimbabwe in the ARROW

## clinical trial



\*Victor Musiime<sup>1</sup>, Adrian Cook<sup>2</sup>, Sabrina Bakeera-Kitaka<sup>3</sup>, Tichaona Vhembo<sup>4</sup>, Joseph Lutaakome<sup>5</sup>, Rosette Keishanyu<sup>1</sup>, Andy Prendergast<sup>2</sup>, Sam Lubwama<sup>1</sup>, Val Robertson<sup>4</sup>, Peter Hughes<sup>5</sup>, Kusum Nathoo<sup>4</sup>, Paula Munderi<sup>5</sup>,

Philippa Musoke<sup>3</sup>, Diana M. Gibb<sup>2</sup>

<sup>1</sup>Joint Clinical Research Centre, Kampala, Uganda ; <sup>2</sup> Medical Research Council, Clinical Trials Unit, London, UK; <sup>3</sup>Paediatric Infectious Diseases Clinic, Mulago hospital, Kampala, Uganda; <sup>4</sup> University of Zimbabwe, Harare, Zimbabwe; <sup>5</sup>Medical Research Council/Uganda Virus Research Institute, Entebbe, Uganda

### BACKGROUND

•Bacteraemia is a common cause of morbidity and mortality in HIV infected children [1, 2]; the commonly isolated pathogens including: S. pneumoniae, S. aureus and Enterobacteriaceae [2, 3, 4]

•Most isolates are susceptible to cephalosporins but high rates of resistance to

cotrimoxazole and penicillin have been observed [2, 4]

•Data on patterns of the bacteraemia pathogens and their antimicrobial sensitivity patterns

still limited

1. Berkley JA, et al. N Eng J Med.2005 Jan 6; 352 (1):39-47 2. le Roux DM, et al. Pediatr Infect Dis J. 2011 May 12 [Epub] 3. Feikin DR, et al. BMC Infect Dis. 2010 Jun 23; 10:186 4. Byam PR, et al. West Indian Med J. 2010 Jul; 59(4): 386-92

#### METHODS

- · ARROW is a randomized trial investigating first-line treatment and monitoring strategies in 1207 previously untreated HIV-1-infected children initiating ART
- Most children had received *haemophilus influenzae type B* vaccination as part of the EPI schedule. None had received pneumococcal vaccination
- Children developing febrile illnesses in follow-up were investigated for infections including blood culture and sensitivity done according to standard microbiological techniques

## RESULTS

•848 blood cultures obtained from 461 children >123 (14.5%) from 105 children were positive •Among children with positive isolates: ≻54/105 (51%) were girls ▶ median age was 4 (range: 0.5 - 15) years



		Susceptibility of other bacterial isolates other than S. pneumonae						
		isolates	Percentage of susceptible isolates					
/	Drug		S. Aureus (N=11)	Salmonella spp (N=6)	<i>E.Coli</i> (N=5)	P.Aeruginosa (N=6)	K.Pneumoniae (N=6)	
	Ceftriaxone		55.6	100	100	100		
	Cefotaxime		100	100	100		0	
	Carl	bapenems	-	100	100	100	66.7	
	Ciprofloxacin		100	100	-	100	100	
/	Gentamicin		0	75	66.7	100		
ĺ	Chloramphenicol		100	-	-	0	0	
	Ery	thromycin	42.9	-	-	-		
	P	enicillin	50	25	0	0	0	
	Cotr	imoxazole	16.7	33	0	50	-	



e e e e e e e e e e e e e e e e e e e								
Susceptibility of Streptococcus pneumoniae								
Name of Antibiotic	Number of susceptible isolates (percentage)							
Vancomycin	16/16 (100)							
Chloramphenicol	6/6 (100)							
Clindamycin	6/6 (100)							
Cefuroxime	4/4 (100)							
Erythromycin	15/16 (93.8)							
Amoxicillin	8/9 (88.9)							
Ceftriaxone	30/36 (83.3)							
Ampicillin	5/6 (83.3)							
Amoxicillin/ clavulanic acid	4/5 (80)							
Penicillin G	8/11 (72.7)							
Oxacillin	8/12 (66.7)							
	24/36 (66.7)							
Cotrimoxazole	10/22 (45.4)							
Gentamicin	1/5 (20)							

#### CONCLUSIONS

•High rates of proven bacteraemia were observed during the first year on ART in African HIVinfected children

•Streptococcus pneumoniae was most commonly isolated, suggesting a need for effective prophylactic antibiotics and/or pneumococcal vaccination

•High rates of resistance to commonly used antibiotics suggest that newer agents like ceftriaxone should be the drugs of choice when treating HIV-infected children with possible bacteraemia

#### COLLABORATORS and ACKNOWLEDGEMENTS

We thank all the ARROW trial participants and their carers, The ARROW Trial team: Trial Steering Committee: I Weller (Chair), E Luyirika, H Lyall, E Malianga, C Mwansambo, M Nyathi, A Wapakhabalo, DM Gibb, A Kekitinwa, Data Monitoring Committee: A Breckenridge (Chair), C Giaquinto, C Hill, J Matenga, J Tumwine Endpoint Review Committee: T Udler (Chair), E Luyirika, H Lyall, E Malianga, C Mwansambo, M Nyathi, A Wapakhabalo, DM Gibb, A Kekitinwa, DM Gibb Joht Clinical Research Centre, Kampala, Uganda, P Mugyenyi, V Muslime, P Mu DM Gibb Joht Clinical Research Centre, Kampala, Uganda, P Mugyenyi, V Muslime, V D Afayo, E Bagurentozi, M Nosenyi, B Nosenyi, B Nosenyi, M Steronyan, J Descentha, J Techtyabhiri, CS Tummisme, R Kelamyu University, Carlon Chairo, B Karagarentozi, M Nesnyang, D Mogibb, A Kekitinwa, J Namusanie, R Karagarentozi, M Nesnyang, D Mogibb, A Kekitinwa, J Namusanie, R Karagarentozi, M Nesnyang, D Mogibb, A Kekitinwa, J Namusanie, R Karagarentozi, M Nesnyang, D Mogibb, A Karagarentozi, M Nesnyang, D Mogibb, J Matama, J Namusanie, R Kalenbar, Katuramu, JH Kyarinpa, J Lutankome, J Matama, M Musingard, G Nabulime, A Ruberantwari, R Schukyn, IM Swekamatte, G Jushabe, D Wang Brythe-Ignanda, Paentarier Infections Disease Centre, Nulage Hospital, Uganda Katuka, J Aselle, J Santaka, G Musoba, SJ Mutebi, J Nakafaero, S Nakyanzi, R Namudue, S Senambo, Victoria Sebudde, S Ssenyonjo, A Wanyoto MRC Clinical Trials Unit, London, Cook, JM Crawley, AA Ferrier, B Naidon, M Syper, AS Walker, A Prendergast, J Crawley Gaussonit/Khulle of the trial d drug nwa, P Mugyenyi, P Munderi, KJ Natho P Musoke, P Nahirya-Ntege, JM Crawle umba, TK Najjuko, E Natukunda, M uit, B Zapasi, J Gumbo, C Katanda, R <sup>1-kirwa</sup>-Ntege, M Aber, FN Kaggwa, P Gibb, MJ Th

Funding: ARROW is funded by the UK Medical Research Council and the UK Department for International Development (DfID). Trial drugs are provided by GlaxosmithKlim