WEPE0616

Ethical and Practical Constraints to the Participation of HIV-infected Orphaned Children in a Clinical Trial in Zimbabwe

Experience from the **A**nti**R**etroviral **R**esearch f**O**r **W**atoto (**ARROW**) Trial

*Contact details:
Department of Paediatrics and Child Health
University of Zimbabwe
Medical School, Box A178
Avondale, Harare, Zimbabwe
Tel: +263 4 791631 ext:2224
Fax: +263 4 700877/797995
Email: mbwakura@medsch.uz.ac.zw

MRC Clinical Trials Unit
222 Euston Road, London, NW1 2DA
Tel: +44 20 7670 4738
Fax: +44 20 7670 4818
Email: jane.crawley@ctu.mrc.ac.uk

AUTHORS: MF Bwakura-Dangarembizi [1], V.Musiime [2], S.Bakeera-Kitaka [3], P.Nahirya-Ntege [4], J.Crawley [5], P.Mugyenyi [2], P.Musoke [2], P.Munderi [3], M.Thomason [5], A.Kekitiiinwa [2], K. Nathoo [1] and the ARROW trial team

[1]University of Zimbabwe-College of Health Sciences, Harare, Zimbabwe; [2]Joint Clinical Research Centre, Kampala, Uganda; [3]Baylor-Uganda, Paediatric Infectious Disease Centre, Mulago Hospital, Kampala, Uganda; [4]MRC/UVRI Programme on AIDS, Entebbe, Uganda; [5]Medical Research Council, Clinical Trials Unit, London, United Kingdom

BACKGROUND

- Clinical trials in children are governed by the Nuremberg Code, which requires informed consent for participation in clinical research, and by the Declaration of Helsinki, which requires proxy consent on behalf of minors from their legally authorized representative
- Institutional Review Boards (IRBs) have responsibility for ensuring that the rights and welfare of subjects are fully protected
- ARROW is a randomised clinical trial evaluating strategies for the management of Anti-Retroviral Therapy (ART) in 1200 HIV-infected children from sites in Uganda (n=800) and Zimbabwe (n=400) (see poster MOPE0191)

ISSUES

ETHICAL CONSTRAINTS

PROBLEMS

- Approximately 40% of HIV-infected children in Zimbabwe are orphaned
- Relatives offer, or are asked, to act as informal guardians
- It is not the cultural norm to legalise this guardianship process, which is lengthy and costly
- The Zimbabwean IRB stipulates that consent is obtained from the child's legal representative
- As a result, orphaned children were excluded from ARROW

SOLUTIONS

- Representation was made to the IRB, which waived the 'legal' requirement
- Guardians were asked to sign an affidavit stating that they understood the high level of care-giver commitment required by ARROW
- Orphaned children are now recruited to ARROW

PRACTICAL CONSTRAINTS

PROBLEMS

- The success of ART depends largely on adherence to medication
- Orphaned children may live with different relatives at various times, and changes in care-giver can lead to a reduction in drug adherence
- Changes in care-giver may also impact upon clinic attendance and confidentiality

SOLUTIONS

- Pill boxes will now be supplied for all children in ARROW to help care-givers administer study medication at the correct time
- Home visitors and counsellors on the ARROW team are available to advise and discuss with children and care-givers issues arising
- The ARROW team has established a support group for orphans and other HIV-infected children, so that practical and psychosocial problems can be addressed, and experiences shared

LESSONS LEARNED AND NEXT STEPS

- Researchers should familiarise themselves with local IRB requirements for consent involving orphans
- IRBs need to be aware of the implications of orphan status on consent for clinical trials
- Groups providing community advice are a vital way to supporting the children and care-givers participating in clinical trials

COLLABORATORS and ACKNOWLEDGEMENTS

We thank all the patients and staff from all the centres participating in the ARROW trial.
Trial Steering Committee: I Weller (Chair), A Kekitiinwa, DM Gibb, E. Malianga, E Luyirika, H Lyall, KJ Nathoo, M Kline, M Nyathi, P Munderi, P Mugyenyi, A Wapakhabulo
Data and Safety Monitoring Committee: A Breckenridge (Chair), C Hill, J Tumwine, I Pazvakavambwa, C Giaquinto
Endpoint Review Committee: G Tudor-Williams (Chair), DM Gibb, JM Crawley, G Ndeezi, H Barigye, HA Mujuru, MF Bwakura-Dangarembizi, P Nahirya-Ntege, P Musoke, V Musiime
Joint Clinical Research Centre, Kampala, Uganda: P Mugyenyi, V Musiime, S Mubokyi, E Natukunda, M Ssenyonga, M Ndigendawani, SO Nsiyona, C Karungi, K Robinah, F Odongo, M Mutumba, J Tezikyabbiri, P Erimu, CS Tumusiime, F Nghania, D Mwebesa, WS Namala, J Bwomezi, R Nadugwa, H Kizito
University of Zimbabwe, Harare, Zimbabwe: KJ Nathoo, MF Bwakura-Dangarembizi, F Mapinge, M Phiri, T Mhute, T Vhembo, MM Sengayi, S Mudzingwa, D Nyoni, R Mandidewa, C Marozva, C Katanda, R Dzapasi, MM Chipiti, D Muchabaiwa, J Steamer, J Gumbo
MRC Programme on AIDS/Uganda Virus Research Institute, Entebbe, Uganda: P Munderi, P Nahirya-Ntege, M Musinguzi, R Katuramu, J Lutaakome, M Aber, R Sebukyu, G Nabulime, IM Ssekamatte, FN Kaggwa, JH Kyalimpa, G Tushabe, D Wangi, L Matama, A Ruberantwari, P Kaleebu
Baylor-Uganda, Paediatric Infectious Disease Centre, Mulago Hospital, Uganda: A Kekitiinwa, P Musoke, S Bakeera-Kitaka, P Kasirye, JK Balungi, B Mugisa, R Ankunda, S Ssenyonjo, J Asello, C Kiiza, G Kaps, J Nakafeero, A Wanyoto, C Semambo, SJ Mutebi, G Musoba, C Mukasa, R Namuddu
MRC Clinical Trials Unit, London, UK: J Darbyshire, A Babiker, DM Gibb, MJ Thomason, JM Crawley, AD Cook, AS Walker, B Naidoo, AA Ferrier, MJ Spyer, AJ Glabay, M Rauchenberger, CJ Spencer-Drake
Funding: ARROW is funded by the UK Medical Research Council and the UK Department for International Development (DfID). Drugs are provided by GlaxoSmithKline