Virological, immunological and toxic effects of highly active antiretroviral therapy in adult HIV-1 infection

Ulrik William Bak Dragsted

This PhD dissertation was accepted by the Faculty of Health Sciences of the University of Copenhagen, and defended on August 15, 2003.

Official opponents: Bente Klarlund Pedersen, Svend Stenvang Pedersen, and Steffen Thirstrup Pedersen.

Tutor: Jens D. Lundgren.

Correspondence to: Ulrik William Bak Dragsted, CHIP, Department 044, H:S Hvidovre University Hospital, Kettegård Allé 30, DK-2650 Hvidovre. E-mail ubd@cphiv.dk

Dan Med Bull 2004:51:128.

ABSTRACT

The PhD dissertation was carried out during employment as clinical research associate at Copenhagen HIV Programme (CHIP), H:S Hvidovre University Hospital. The primary objective of the dissertation was to assess the efficacy and safety of highly active antiretroviral treatment (HAART) of HIV-1 infection in adults. The dissertation is based on (interim) results of randomised, international, open-label, phase III & IV, clinical trials and one large pan-European cohort study.

There is a need for new treatment modalities with the ability to lower the risk of developing side effects from and increase adherence to HAART, and at the same time maintain or even increase the efficacy of first and subsequent HAART regimens. Included in the dissertation are comparative trials, which for the first time are assessing the virological and/or immunological and/or clinical and toxicological aspects of pharmacological protease inhibitor-enhancement (boosting) (MaxCmin1 & 2), continued treatment with an antiretroviral agent to which the patient is harbouring resistant virus (COLATE), and antiretroviral treatment with or without adjunctive intermittent interleukin-2 (ESPRIT). Further, predictors of immunological failure following initial immunologic response were investigated (EuroSIDA). The trials have, and are expected to continue to have, influence on clinical treatment practice as well as the conduct of publicly funded investigator initiated, international (HIV-1) trials.