Journal of the International AIDS Society

Keynote presentation

How will we use the new ART drugs?

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from Ninth International Congress on Drug Therapy in HIV Infection
Glasgow, UK. 9–13 November 2008

Published: 10 November 2008

Journal of the International AIDS Society 2008, **11**(Suppl 1):K2 doi:10.1186/1758-2652-11-S1-K2

This abstract is available from: http://www.jiasociety.org/content/11/S1/k2

Combined antiretroviral therapies have revolutionized the prognosis of HIV disease transforming an almost uniformly lethal disease into a chronic one with an estimated survival of several decades on effective antiretroviral therapy. However, several issues had tempered this 'idyllic' situation: cART cannot be stopped without damages such as increases in number of deaths and co-morbidities even at relatively high ratio of CD4 demonstrating that HIV is not only deleterious by its consequences on immune deficit but also in the fact that it promotes high immune activation that follows the rebound in HIV replication – cART at least NRTIs and PIs, is associated with toxicities and co-morbidities. This leads us to investigate different drug-class sparing maintenance strategies opening a new field of research. PI monotherapy is currently investigated mainly with lopinavir or darunavir under investigation in two randomized studies – MONET in Europe and MONOI in France through the ANRS network with results available in 2009. The development of new classes of drugs had already brought significant improvement in HIV disease management. Integrase inhibitors mainly the recently licensed raltegravir had led to increase in the rate of full viral suppression in salvage patients in combination with new drugs from old classes such as darunavir or etravirine and allowed up to over 80% of plasma HIV-RNA <50 copies/ml. Inhibitors of coreceptors CCR5, mainly maraviroc are not only antiretroviral agents but also an immune modulatory agent with specific action on CD4 lymphocytes, immune activation or potentially on apoptosis. Because these drugs act on different viral targets, because of their different resistance and toxicity profile from NRTIs or PIs, clinical research has to explore their potential role in the treatment gaps. Several important questions throughout remain to be explored: – What is the role of these new drugs in primary infection? – How can both raltegravir with its very rapid decrease in viral load and maraviroc with its action on CD4 decrease the delay needed time to control the virus and the time to restore CD4 above 200/mm3 in late HIV presenters? – How can these drugs be used in maintenance therapy in patients with undetectable viral load but a long history with subsequent toxicities of PIs or NNRTIs? – Can we limit the number and the burden of drugs used to control viral replication? – Will these drugs in addition to classic cART be capable to decrease viral reservoirs and why not tends towards eradication?