EDITORIAL

stARTing cART now! HIV treatment Italian Guidelines Update Dec. 2014

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The December 2014 edition of the Italian Guidelines for the use of antiretroviral agents and the diagnosis-clinical management HIV-1 infected persons (GL) (HIV/AIDS Italian Expert Panel, 2014) were drawn up under the mandate of the Ministry of Health by the Istituto Superiore di Sanità (National AIDS Centre), in collaboration with the National AIDS Commission, the National Conference of Associations for the Fight Against AIDS (Ministry of Health) and the Italian Society of Infectious and Tropical Diseases (SIMIT). The GL welcome the widespread practice of allowing all people with HIV willing to start combined antiretroviral treatment (cART) to do so.

The choice of this indication was discussed and approved by almost 100 experts who have worked on the GL document in various ways, assessing literature reports prior to the end of May 2015, date of publication of the preliminary results of the (randomized) START (Strategic Timing of antiretroviral treatment) Study, which conclusively established the benefit of early as opposed to deferred initiation of therapy (INSIGHT START Study Group, 2015).

The primary aim of the START Study on naïve and asymptomatic HIV-infected patients was to detect differences in AIDS, non-AIDS serious events or death among those who started cART immediately and those who waited for the threshold of 350 cells/mm^3. The difference between the two groups of 41 versus 86 events detected in the follow-up of 3 years is the main reason underpinning the decision of the Data Safety Monitoring Board (and the sponsor, the National Institute of Allergy and Infectious Diseases - NIAID) to provide immediate treatment to everyone.

It is not the first time (but we hope it will be the last!) that strategic randomized trials demonstrate after a long time that decisions taken by experts - based on expertise, good clinical practice, "non randomized" evidence, social and health reasons - are correct.

It should be noted that with regard to Italy, the feared impact this recommendation would have in terms of an uncontrolled rise in costs of antiretroviral drugs is proving to be quite marginal and limited, as the experts had already estimated, for the following reasons:

1) The low percentage of people diagnosed and therefore naïve per year with more than 500 CD4 cells/mm^3 (10% of new infections).
2) The very high percentage of those who remain in the *continuum* of care.
3) The very high percentage of people with HIV on treatment (90%).
4) The fact that similar, if not even more stringent recommendations, contained in other national guidelines (eg., United States, Spain) have certainly not caused (additional!) financial crises in their respective countries, despite the prevalence of more expensive drugs among the recommended initial regimens.

Considering the well-established clinical practice in Italy of *personalized treatment schedules* and *long-term therapeutic strategies* (e.g.: induction/maintenance, simplification, etc.), we

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do not believe in a blind implementation of the above indications without an accurate individual assessment of the cost/benefit ratio.
The Italian GL reaffirm the need to watch over early detection of comorbidities, especially in those who have an undetectable viral load, where the residual viraemia is a target through advanced diagnostics not only as it relates to the usual viral load (HIV RNA ultrasensitive), but also to the total virus. In the near future we will have standardized data on HIV DNA important to predict the evolution/progression of infection (failures, resistances, reservoirs, etc.). Unfortunately, even the latest guidelines are not yet in a position to provide specific guidance for the treatment of people with HIV who are diagnosed late (advanced naïve, i.e. with less than 50 CD4 cells/mm^3 and over 500,000 copies/mL HIV RNA), a condition in which the standard of care available today appears the most unsatisfactory. Filling the lack of information in a setting with such clear biological assumptions of high risk of treatment failure (invasion of the reservoir, onset of resistances, persistent viraemia, opportunistic infections, IRIS) is a priority for the scientific community.
Finally, all the measures aimed at better control of viraemia in a population (HIV positive people in Italy) with a high continuum of care compliance rate can only help reduce the risk of transmission of infection in a nation that does not excel in prevention policies for sexually transmitted diseases.

REFERENCES

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