Access to antiretroviral therapy for people living with HIV/AIDS in resource-limited countries has greatly improved in recent years, but is not yet optimal. The rising number of patients on antiretrovirals does, however, raise the increasingly urgent question of treatment failure after first- and second-line treatment. In patients in this situation, HIV resistance mutations are frequent and often involve drug cross-resistance. The question then is to know which antiretroviral therapy can be proposed third line, in a context of limited access to measurement of viral load (to identify virologic failure) and especially to genotypic tests (which identify resistance mutations).

The treatment cohort ANRS 12269-THILAO (THird Line Antiretroviral Optimization) was designed to explore a third-line therapeutic strategy in patients with virologic failure after second-line triple-drug therapy. Launched in March 2013, this study in 201 patients in four West African countries (Burkina Faso, Ivory Coast, Mali, and Senegal) was jointly overseen by Prof Serge Ehólié (ANRS Ivory Coast Site, CHU de Treichville) and Dr Roland Landman, Hôpital Bichat, AP-HP, Paris, and Institut de Médecine et d’Épidémiologie Appliquée, Paris, working with their colleagues at Inserm and AP-HP. Dr Raoul Moh (ANRS Ivory Coast Site) will present the results on 24 July in an oral communication, during the 9th IAS Conference on HIV Science, organized by the International Aids Society and the ANRS in Paris.

Whether first- or second-line, the treatment of these patients was in line with World Health Organization (WHO) recommendations. Two successive interventions were planned in these patients with treatment failure. First, adherence was increased in all patients by means of a series of measures (pill organizers, phone reminders, support group, etc.). The patients continued their second-line treatment for 4 months, after which viral load was measured to decide on treatment:

- Maintenance of second-line triple-drug therapy in patients in whom viral load is undetectable.
- Switch to third-line antiretroviral therapy in patients with confirmed virologic failure. The new treatment comprised the latest antiretrovirals not yet taken by the patients: darunavir boosted with ritonavir (protease inhibitors) and raltegravir (integrase inhibitor).
In both cases, the patients were followed up for an additional 48 weeks.

After the 4 months during which measures were implemented to increase adherence, 66% of the patients were able to maintain their second-line treatment, their viral load again being undetectable. “This indicates that most patients considered to be with virologic failure were not really,” explain Dr Landman and Prof Eholié. “The patients had, in fact, difficulty adhering to treatment. This led the clinicians to act on adherence before deciding on treatment.”

Among the patients who took third-line antiretroviral treatment, 62 % had an undetectable viral load after 48 weeks. No serious side effect was observed. These findings show that it is possible to achieve good efficacy with third-line antiretroviral therapy in resource-limited countries.

Prof François Dabis, Director of the ANRS, notes that the “ANRS 12269-THILAO confirms the need to improve adherence in a lasting fashion, that is to say for life. It also provides firm evidence that third-line treatments should be accessible in resource-limited countries to patients who, despite these efforts, have experienced treatment failure.”

Lastly, these results also raise questions concerning therapeutic strategy in the case of lack of viral control. Prof Eholié and Dr Landman point out that “It is essential we review the way viral load is used in resource-limited countries, so as to avoid prescription of the latest antiretroviral drugs, which are far more costly than older antiretrovirals. This is a public health challenge for all resource-limited countries.”

Source:
48-weeks efficacy of a third line based on darunavir plus raltegravir regimen in HIV-infected adults who failed second-line protease inhibitor based-regimen in Sub-Saharan Africa, ANRS 12269 THILAO study.


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