

## **Therapeutic Application of Antiviral Resistance Testing**

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HIV is a highly evolving virus. Put under antiviral pressure, it has an extraordinary ability to generate mutations that can cause resistance to antiviral drugs. This resistance to a specific drug can be cross-reacting with other drugs of the same class, thus causing the loss of an entire class of antivirals.

Resistance to antivirals has been associated to loss of therapeutic options, clinical progression, and death. Even with the most modern therapies, resistance still represents a substantial risk, particularly in the frame of a long-term therapy. Indeed, cure of HIV is today impossible, therefore therapy needs to be planned for life. In these conditions, and with the limited amount of new drugs coming, viral load needs to be maintained undetectable as long as possible, in order to preserve therapeutic options, avoid the development of resistance, and limit the risk of clinical progression. Resistance may occur also at low copy number, and whenever viral replication occurs under the pressure of antivirals. For this reason, the early use of the best drugs available, and the maintenance of undetectable viral load, represent the goal of a therapeutic strategy aimed for life. By contrast, positive viremia, even at low copy number, indicates an increased risk of failure, and therefore suggests to consider as soon as possible a therapeutic change.

In order to increase the chances of success of the first and following therapeutic regimens, resistance test should be widely used (in all conditions in which they are recommended by international guidelines), to select the drugs with highest chance to be effective, taking into account also viremia, the presence of resistance-associated mutations, CD4, and the clinical situation of the patient.

In conclusion, the proper use of resistance test, as well as of other diagnostic testings, is a key tool to maintain the virus under control as long as possible.