

### Resistance tests

Resistance testing has been used in HIV research to increase our knowledge on how resistance to anti-HIV drugs develops. It is also being used in clinics to choose the most appropriate treatment for each patient. It is advisable that these tests are done whenever you are changing your drug combination.

It takes time to obtain the results of resistance tests. They are hard to perform and interpret and standardisation and quality control can be lacking. In addition, they can't be done if someone's viral load is below 200 copies/ml.

However, if you know the results of a resistance test before changing your therapy, it is more likely that you will have a more successful viral-load response to your new treatment (at least over the short- and medium-term) than people who switch treatment without this information.

#### Types of resistance tests

There are two methods of testing for drug resistance:

- **Genotypic tests:** these identify specific changes, or mutations, in HIV's reverse transcriptase or protease genes. These are linked to resistance to anti-HIV drugs.
- **Phenotypic tests:** these measure the concentration that a drug should achieve in order to reduce viral replication. When resistance to a drug begins to develop, higher levels of that drug will be needed to stop the virus growing.

Currently, there is no clear indication that one type of test is more useful than the other. Each has advantages and disadvantages. However only genotypic tests are performed out of investigational settings.

#### Genotypic tests

The advantage of this type of test is that results are available relatively quickly (in 4-5 days). These tests are simpler to do, they don't require highly skilled staff and they are predictive (this means their results can show up the possibility of future resistances developing). They can also be done in healthcare settings such as clinics

and hospitals. The disadvantages are that they only measure resistance indirectly, they are complex to interpret and they cannot be done at viral levels below 200 copies/ml.

#### Phenotypic tests

The advantages of phenotypic tests are that they measure directly the sensitivity of the virus to a drug, and that their results are relatively easy to interpret. The disadvantages are that results can be slow (2-3 weeks), they are more expensive (costing twice as much as genotypic tests), they require complex laboratory equipment and the fact that they cannot be done at viral levels below 200 copies/ml neither. Currently, they are only performed in clinical research settings.

#### Guidance on resistance tests

- Resistance tests are a relatively new tool in HIV care. Their results should be interpreted and explained by someone who is experienced in using them.
- Test results should be considered alongside a full treatment and care history, rather than in isolation. This is because resistance is not the only reason why drugs fail: lack of adherence, poor absorption and drug interactions are other possible causes.
- Resistance tests cannot be done if your viral load is below 200 copies/ml.
- Resistance tests are more accurate when performed before changing or stopping a failing combination. This is because resistant viruses will be replaced by a virus population sensitive to drugs in a few weeks after you stop taking your current drugs. Commonly, resistant viruses are less able to replicate than sensitive viruses, so resistant viruses that once predominated will then become

one of many sub-groups of viruses in your body. Most tests are unable to detect sub-groups which form less than 10-20% of your viral population. Restarting a drug to which a pool of your viruses is resistant will allow this group to grow predominant again, causing the treatment to fail.

- One of the most important times to test for resistance is just before you start anti-HIV treatment. If you were infected with a virus resistant to one of the drugs in your first combination, your treatment may fail quickly. However, when we are considering a chronic infection (more than six months after acquiring the virus), the results of a resistance test before starting treatment are more difficult to interpret than in the case of people who are shifting their combinations. This is because, viral populations usually evolve over the time and resistant viruses may become only a small minority of the total population, making them very difficult to detect

before starting treatment (although some viruses, like the ones resistant to AZT can sometimes be detected long after infection). Worthy of note is that once started the therapy, resistant viruses can grow quickly and become detectable in resistant tests.

- Resistance tests may be particularly helpful when choosing treatment options in people very recently infected, since resistant viruses will still be present at this point.
- Current Spanish treatment guidelines recommend that resistance tests should be used at the point of HIV diagnosis, before starting treatment and before any change of the drug combination.

This fact sheet offers basic information on the tests designed to measure viral resistance to anti-HIV drugs. If you want to know more on resistance, see *InfoVIHtal #46 Resistance development*.



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