Winnipeg doctors use dolutegravir and darunavir for simplifying treatment

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- People diagnosed with drug-resistant HIV are prescribed complex treatment
- Winnipeg doctors switched 22 such patients to a simplified but potent regimen
- All patients tolerated the regimen and maintained undetectable viral loads

Over the past several years, doctors in Winnipeg have diagnosed people with HIV who required a complex regimen for their initial HIV treatment (ART). The reason for this unusual treatment in first-line therapy was that genetic analysis of their HIV found that it was wholly or partially resistant to the widely used nuke (nucleoside analogue) tenofovir as well as other members of this class of drugs. However, none of them had HIV that was resistant to other classes of anti-HIV drugs such as protease inhibitors or integrase inhibitors. Based on the resistance testing of their patients’ virus, the doctors cobbled together complex regimens such as the following:

- darunavir + low-dose ritonavir + etravirine (Intellence) + dolutegravir (Tivicay)
- Genvoya (elvitegravir + cobicistat + TAF + FTC) + darunavir
- darunavir + low-dose ritonavir + etravirine + raltegravir

In some cases, these regimens involved taking up to six pills a day and cost between CAN $2,100 and $2,400 per patient per month.

Patients who achieved and then maintained an undetectable viral load for 12 consecutive months with these initial regimens were then offered a simplified but still potent regimen. The decision to switch to the simplified regimen “was made by patient and clinician consensus,” according to the doctors. Of the 25 patients who were put on complex initial regimens, 22 achieved and maintained undetectable viral loads. Among these 22 patients, 13 agreed to switch to the following regimen:

- darunavir 800 mg + ritonavir 100 mg + dolutegravir 50 mg

With this combination, dubbed the “double D” regimen by the doctors, all drugs were taken once daily. The low dose of ritonavir is meant to raise and maintain darunavir levels in the blood so that once-daily dosing can be achieved. When used in this way, ritonavir does not have antiviral activity against HIV. It is darunavir (a potent protease inhibitor) and dolutegravir (a potent integrase inhibitor) that are doing the work of keeping HIV suppressed. This non-standard combination is powerful and, if adherence is good, should work for many years.

All patients tolerated the new regimen; no side effects have been reported over a year of monitoring. Furthermore, patients continued to have undetectable viral loads for at least one year after making the switch to the “double D” regimen. These results from Winnipeg are encouraging and are supported by studies from Europe. It would be great if the Winnipeg team continued to monitor these patients and could submit long-term results from the “double D” regimen in several years.

In Italy

Researchers at clinical centres in Milan, Florence, Genoa and other parts of Italy have also used the combination of darunavir + ritonavir + dolutegravir in 130 HIV-positive patients who wanted/needed to change their existing regimen mostly because of the following issues:
• regimen simplification
• virological failure
• side effects

Patients received one of the following two regimens:

- darunavir 800 mg + ritonavir 100 mg + dolutegravir 50 mg; all drugs taken once daily - 113 people
- darunavir 600 mg + ritonavir 100 mg + dolutegravir 50 mg; all drugs taken twice daily - 17 people

The researchers used several different assays to measure viral load in blood samples, including the following:

- Abbot HIV-1 RT-PCR, with a lower limit of 37 copies
- COBAS TaqMan HIV-1 Test, with a lower limit of 20 copies
- A single copy assay, with a lower limit of 1 copy; values below this were interpreted as “no virus detected.”
  Note: In cases where the single copy assay returned with a result of less than 1 copy (“no virus detected”),
  this does not mean patients were cured, as only blood samples were tested. The vast majority of HIV is within
  lymphocytes and other cells of the immune system and these cells are largely in the lymph nodes, spleen and
  some fatty tissues. Also, there are cells of the immune system guarding key organ-systems against germs, so
  tissues such as the lungs, kidneys, liver and brain will also contain HIV-infected cells.

After one year on these regimens, the virological results were as follows:

- 76% had “no virus detected” (less than 1 copy/mL)
- 15% had a viral load between 1 and 49 copies/mL
- 6% had a viral load of 50 copies/mL or greater

(The total does not equal 100% because four participants dropped out.)

The researchers did not find that participants had significant neurological side effects as have been reported by
some study centres in other parts of Europe that prescribed standard regimens containing dolutegravir (that is, a
combination of dolutegravir and two nukes).

In Germany

Researchers at several clinics in Germany, including in Munich, Berlin, Cologne and Bonn, are conducting a 320-
person randomized study called DUALIS. In this study, researchers are comparing the safety and effectiveness of
the following combinations taken once daily:

- darunavir + ritonavir + dolutegravir
- darunavir + ritonavir with either Truvada (TDF + FTC) or Kivexa (abacavir + 3TC)

A sub-study with 10 participants (seven men and three women) was done to measure the levels of dolutegravir and
darunavir in the blood when taken with food. Researchers found that the drugs were well absorbed and that levels
of the drugs were “adequate” to suppress HIV.

DUALIS is expected to be completed later in 2018 and will hopefully provide robust data about the “double D”
regimen.

——Sean R. Hosein

REFERENCES:

   transmitted HIV thymidine analog resistance in Manitoba, Canada. *International Journal of STD and AIDS*.
2. Capetti AF, Cossu MV, Orofino G, et al. A dual regimen of ritonavir/darunavir plus dolutegravir for rescue or
   simplification of rescue therapy: 48 weeks' observational data. *BMC Infectious Diseases*. 2017 Sep
   30;17(1):658.
   darunavir in HIV patients: the DUALIS study. *Journal of Antimicrobial Chemotherapy*. 2017 Sep
   1;72(9):2679-


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