A study from Paris about switching to dolutegravir monotherapy

Doctors in Paris conducted a study whereby participants whose current regimen resulted in an undetectable viral load in their blood (less than 50 copies/mL) could be switched to dolutegravir 50 mg once daily.

Between May 2014 and January 2015, 28 participants were recruited and had the following average profile at the start of the study:

- age – 48 years
- no data on gender were released
- years taking ART – 17
- years with a viral load less than 50 copies/mL – 7
- CD4+ cell count – 624 cells/mm$^3$

During the first 24 weeks of the study, participants had blood drawn at regular intervals for extensive analysis. Researchers presented 24 weeks of data and plan to continue to monitor participants.

**Results**

For the first 12 weeks of the study, all participants maintained a viral load less than 50 copies/mL. Furthermore, using a more sensitive test, researchers found that nearly all participants maintained a viral load less than 20 copies/mL up to the first 12 weeks. On or after that time point, three participants developed virological failure (details about this appear next). Investigating these cases and trying to find the cause of virological failure is important because trials are planned that seek to test simplified regimens containing dolutegravir.

**Case 1**

Prior to the present study, a 35-year-old woman had taken darunavir (Prezista) + low-dose ritonavir (Norvir) + Truvada (tenofovir + FTC). This had resulted in her viral load being less than 50 copies/mL. In the past she had used a combination of two drugs, etravirine (Intelence) + the integrase inhibitor raltegravir (Isentress). At the start of the present study her CD4+ count was 525 cells/mm$^3$.

In the 12$^{th}$ week of the study her viral load became detectable, reaching 136 copies/mL. She continued taking dolutegravir monotherapy and by the 24$^{th}$ week of the study her viral load had climbed to 2,220 copies/mL.

The amount of dolutegravir in her blood throughout the study was usually within the expected range, suggesting good adherence. However, as seen by her viral load in week 24, HIV had developed a degree of resistance to all integrase inhibitors, including dolutegravir. Faced with her increasing viral load, doctors doubled her dose of dolutegravir to 50 mg twice daily (the dose used to treat treatment-experienced patients) and added Truvada to her regimen. This reduced her viral load back to undetectable. Using a more sensitive test, her viral load was less than 20 copies/mL.

**Case 2**

This was a 56-year-old man who had taken different regimens for the past 18 years. For seven months prior to entering the present study, his regimen was Stribild, which contains the integrase inhibitor elvitegravir. His CD4+ count was 1,108 cells/mm$^3$.

The man’s viral load while on dolutegravir monotherapy was less than 50 copies/mL and also less than 20 copies/mL.
when tested with an ultrasensitive assay. However, in the 12th week of the study, his viral load rose to 138 copies/mL. He remained on monotherapy and his viral load rose to 469 copies/mL in week 13. Analysis of his blood revealed that HIV had developed a moderate degree of resistance to raltegravir and elvitegravir, and therefore to dolutegravir as well.

Doctors changed his regimen, increasing his dose of dolutegravir to 50 mg twice daily and adding Truvada. This helped re-suppress his viral load to less than 20 copies/mL by the 24th week of the study.

**Case 3**

This involved a 57-year-old man who had been taking a combination of raltegravir + Truvada for six years prior to entering the study. During that time his viral load was generally less than 20 copies/mL. On one occasion it had risen to 37 copies/mL. His CD4+ count was 940 cells/mm$^3$.

For most of the study this man’s viral load was less than 20 copies/mL but by the 24th week it had risen to 291 copies/mL. Analysis of his HIV revealed that it had developed resistance to raltegravir, elvitegravir and dolutegravir. Doctors then gave him a combination of rilpivirine (Edurant) + Truvada. Over the course of 10 subsequent weeks his viral load gradually declined, reaching 43 copies/mL by week 38.

**Caution**

The researchers warn that people who have had previous exposure to integrase inhibitors are not likely to be ideal candidates for dolutegravir monotherapy. This issue arises because the development of strains of HIV with the ability to partially resist integrase inhibitors can occur in some people who use these drugs. Initially at least, these strains may occur at relatively low levels. But when therapy is sub-optimal—that is, when one’s viral load is increasing while they are taking an integrase inhibitor—these strains can become more common and their ability to resist integrase inhibitors intensifies.

Overall, nearly 89% of participants were able to have their viral load stay at less than 20 copies/mL for the duration of the study. The research teams plans to monitor the participants for another six months.

Bear in mind that the Paris study was small and not randomized, so its findings are preliminary at best.

—Sean R. Hosein

REFERENCE:

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