Darunavir shows its strength

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The protease inhibitor darunavir (Prezista, TMC114) has recently been approved for use in Canada and the United States. Darunavir is supposed to be active against strains of HIV that are resistant to other protease inhibitors, so this drug is of particular interest to treatment-experienced PHAs.

Approval of darunavir was based on data collected from clinical trials conducted over a period of six months. In Canada and the U.S., regulatory approval was conditional on long-term data being collected, a process that is now underway. Preliminary analysis of darunavir after one year of use is very promising.

Study details

Two Phase II trials of darunavir—Power 1 and Power 2—were conducted. The purpose of these studies was to compare the effect of different doses of darunavir against that of another protease inhibitor(s) selected by participants’ doctors.

In these trials, darunavir was taken together with a small dose of another protease inhibitor, ritonavir (Norvir). The purpose of ritonavir was to raise and maintain the levels of darunavir in the blood. Participants in these studies had previously used three of the most common classes of HIV medications:

- nukes (nucleoside analogues)
- non-nukes (non-nucleoside reverse transcriptase inhibitors)
- protease inhibitors (PIs)

Prior to entering the Power studies, treatment-experienced volunteers often had a detectable viral load, suggesting that their existing regimen was failing. Researchers randomly assigned participants to one of the following regimens:

- a doctor-selected PI(s) + other anti-HIV agents. These other anti-HIV agents were called an optimized background therapy (OBT).
- darunavir/r 400/100 mg once daily + OBT
- darunavir/r 800/100 mg once daily + OBT
- darunavir/r 400/100 mg twice daily + OBT
- darunavir/r 600/100 mg twice daily + OBT

Although several doses of darunavir were used in these clinical trials, we will focus on results with the approved dose of darunavir/ritonavir: 600/100 mg twice daily.

A total of 131 participants received darunavir/r at the approved dose and 124 other participants received another PI(s). At the start of the study, the average profile of participants from both treatment groups was as follows:

- 11% female, 89% male
- age – 44 years
- length of HIV infection – 12 years
- viral load – 40,000 copies
- CD4+ count – 158 cells

Most participants had an average of eight mutations in their HIV that helped it to resist the effect of other PIs.
**Results—Effectiveness**

There are a number of ways to assess the anti-HIV activity of darunavir/r. The first is to examine the proportion of participants whose regimens failed because of increasing viral loads, suggesting virologic resistance:

- darunavir/r – 8%
- other PI(s) – 67%

A second way to assess the effectiveness of medications is to look at the proportion of participants whose viral load fell below the 50-copy mark and remained that way at the end of the study:

- darunavir/r – 46%
- other PI(s) – 10%

**Results—Changes in CD4+ counts**

After one year, cell counts had increased as follows:

- darunavir/r – an extra 102 cells
- other PI(s) – an extra 19 cells

**Results—Side effects and complications**

Common side effects among darunavir/r users included the following:

- nausea—20%
- diarrhea—20%
- headache—16%
- sore throat—12%
- herpes sores—10%

It is important to note that the diarrhea and nausea were likely caused by the use of ritonavir. That occurrence of herpes outbreaks suggests that, at some point in the study, participants had relatively weakened immune systems—not that these were caused by darunavir/r.

Lab tests showed that darunavir/r recipients were more likely to have higher-than-normal levels of triglycerides and the liver enzyme GGT (gamma-glutamyl transpeptidase).

About 9% of darunavir/r users and 5% of other participants quit the study because of the intensity of side effects. Bear in mind that among treatment-experienced PHAs, particularly those with low CD4+ cell counts, side effects may appear to be more intense.

Overall, these findings confirm that darunavir/r has potent anti-HIV activity and is generally tolerated. Other studies of darunavir/r are ongoing or planned.

**REFERENCE:**

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