From Treatment Update 166

Lopinavir and ritonavir (Kaletra) tablets get tested

Putting more than one medication in one pill is a process called co-formulation. Having more than one medication in a pill reduces the overall number of pills that a person needs to take every day; therefore, co-formulation should result in improved adherence. Co-formulation will become increasingly common in high-income countries as pharmaceutical manufacturers realize that people prefer to take as few pills as possible. The combination of two drugs, lopinavir and ritonavir (Norvir), in one capsule or tablet is called Kaletra. The newer formulation of lopinavir and ritonavir is called the Kaletra tablet, and it has several advantages over the capsule formulation, such as the following:

- it does not require refrigeration
- it can be taken with or without food
- it has a reduced number of pills per day

Researchers in Canada, Spain and the United States conducted a clinical trial called MO5-730. This study enrolled more than 600 people with HIV/AIDS to compare the safety and effectiveness of lopinavir tablets taken once or twice daily to that of the capsules (both formulations taken as part of highly active antiretroviral therapy, or HAART).

The results showed that the tablet formulation was as effective as the capsule formulation. There were no apparent differences in side effects between the capsule and tablet. When questioned, the majority of study participants preferred the tablet formulation. Further details appear below.

Study details

Researchers recruited 664 volunteers who had never previously taken anti-HIV therapy. They randomly assigned the volunteers to one of the following four regimens:

- lopinavir tablets – taken once daily
- lopinavir capsules – taken once daily
- lopinavir tablets – taken twice daily
- lopinavir capsules – taken twice daily

All participants also received the co-formulation of two other anti-HIV medicines, tenofovir (Viread) and FTC (emtricitabine, Emtriva), in one pill called Truvada.

At the start of the study, the average profile of participants was as follows:

- 20% female, 80% male
- age – 39 years
- viral load – 100,000 copies
- CD4+ cell count – 215 cells

Results—one year later

In clinical trials, a proportion of participants leave for many reasons. In this study, about 15% of participants dropped out of the trial. About 5% of participants left the once-daily group because of side effects compared to 3% in the twice-daily group. However, this difference was not statistically significant.

Results—effectiveness

After 48 weeks the proportion of participants with viral loads below the 50-copy mark was as follows:
• once-daily regimen – 77%
• twice-daily regimen – 76%

This difference was not statistically significant. The results suggest that a once-daily regimen of lopinavir tablets or capsules is not worse than a twice-daily regimen of the same drug.

In general, HIV positive people with high viral loads (more than 100,000 copies) may not always respond as well to therapy as people with lower viral loads. However, in the present study, both once- and twice-daily regimens were effective in volunteers with high viral loads.

**Side effects**

Historically, lopinavir capsules are associated with an increased risk of diarrhea. There were hopes that the newer tablet formulation would decrease that risk, however, researchers only collected data on diarrhea during the first eight weeks of the present study and during that time no significant difference in diarrhea was noted between the tablet and capsule formulation. As well, neither once- nor twice-daily dosing seemed to have any significant difference on this side effect.

There were no significant differences among any of the study groups on the following blood tests:

• liver enzymes levels greater than five times above the upper limit of normal
• cholesterol greater than 300 mg/dL
• triglycerides greater than 750 mg/dL
• changes in kidney health

**Focus on lipids**

Levels of total cholesterol, triglycerides and LDL-cholesterol (so-called “bad” cholesterol) did not increase as much in participants taking twice-daily regimens as it did in those taking the drug once daily.

Overall, once-daily lopinavir tablets was not less effective than twice-daily lopinavir. The tablet formulation appears to be similar to the capsule formulation in terms of safety and effectiveness.

**REFERENCE:**

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