The Castle study: lopinavir vs. atazanavir

Drug companies are constantly trying to devise interesting names for clinical trials, and now we present one such study, called Castle, that compared effects of lopinavir/ritonavir to atazanavir (Reyataz)/ritonavir.

Dr. Jean-Michel Molina from Paris, France, presented interim results from a two-year study that enrolled 883 participants who were randomly assigned to one of two regimens:

- atazanavir/r (300/100 mg) + tenofovir 300 mg + FTC 200 mg (440 volunteers)
- lopinavir/r (400/100 mg) + tenofovir 300 mg + FTC 200 mg (443 volunteers)

Note that volunteers taking the first regimen only had to take their pills once daily, while volunteers on the second regimen had to take the lopinavir/r portion of their regimen twice daily.

Also, the co-formulation of tenofovir and FTC was used (Truvada). This was taken once daily. During the first year of the study, participants assigned to the lopinavir/r group used the capsule formulation of that drug. In the second year they received the tablet formulation.

The average profile of participants at the start of the study was as follows:

- 31% female, 69% male
- age – 35 years
- viral load – 100,000 copies
- CD4+ cell count – 200 cells
- 13% of participants were co-infected with hepatitis B or C viruses

The goal of this study was to demonstrate that atazanavir/r is not worse than lopinavir/r.

Results

Results from the first year of the study were presented at CROI. The proportion of participants in each group who had their viral load suppressed (below the 50-copy mark) after one year was as follows:

- atazanavir/r – 78%
- lopinavir/r – 76%

This difference was not statistically significant. It also demonstrates that atazanavir/r is not worse than lopinavir/r.

Among participants who entered the study with a viral load greater than 100,000 copies, the proportion that had their viral load fall below the 50-copy mark after one year in each of the two groups was as follows:

- atazanavir/r – 74%
- lopinavir/r – 72%

Again, this difference was not statistically significant and nor was the difference between the following increases in CD4+ counts:

- atazanavir/r – 203 extra CD4+ cells
- lopinavir/r – 219 extra CD4+ cells

Results—side effects

The proportion of participants who developed side effects of a moderate to life-threatening intensity was as follows:
Jaundice
- atazanavir/r – 4%
- lopinavir/r – 0%

Nausea
- atazanavir/r – 4%
- lopinavir/r – 8%

Diarrhea
- atazanavir/r – 2%
- lopinavir/r – 11%

Rash
- atazanavir/r – 3%
- lopinavir/r – 2%

The sponsor of the study, Bristol-Myers Squibb (BMS), is also the manufacturer of atazanavir. At CROI, BMS only released information on what it termed “selected” side effects. Hopefully, in the future, the complete details on this study will become publicly available.

The proportion of participants who had life-threatening elevations in specific lab tests was as follows:

**Bilirubin (a waste product that can build up in the blood and discolour the skin and eyes)**
- atazanavir/r – 34%
- lopinavir/r – less than 1%

**ALT (a liver enzyme) levels greater than five times the upper limit of normal**
- atazanavir/r – 2%
- lopinavir/r – 1%

**AST (a liver enzyme) levels greater than five times the upper limit of normal**
- atazanavir/r – 2%
- lopinavir/r – 1%

**Total cholesterol 240 mg/dL or greater**
- atazanavir/r – 7%
- lopinavir/r – 18%

**Triglycerides 751 mg/dL or greater**
- atazanavir/r – less than 1%
- lopinavir/r – 4%

**High blood sugar**
- atazanavir/r – less than 1%
- lopinavir/r – less than 1%

Oddly, no data were presented on changes to important lipids such as LDL- and HDL-cholesterol.
There were no significant changes in kidney health during the study.

Results from two years of study should be available in 2009.

Overall, the results from this study suggest that when it comes to suppressing HIV in people new to treatment, atazanavir/r regimens are not less effective than regimens containing lopinavir/r.

**REFERENCE:**

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