Limitations of this study include open-label design and use of 3 capsules twice daily of 1% of 431 patients in the lopinavir/ritonavir group. In none of 437 patients in the lopinavir/ritonavir group. There were grade 3 to 4 increases in treatment-related diarrhea (10 [2%] vs 50 [11%]) and nausea (17 [4%] vs 33 [8%]).

Grade 2 to 4 jaundice occurred in 16 (4%) of 441 patients in the atazanavir/ritonavir group but in none of 437 patients in the lopinavir/ritonavir group. Compared with patients in the lopinavir/ritonavir group, fewer patients in the atazanavir/ritonavir group had grade 2 to 4 resistance to atazanavir.

Serious adverse events occurred in 51 (12%) of 441 patients in the atazanavir/ritonavir group and in 42 (10%) of 437 patients in the lopinavir/ritonavir group. Compared with patients in the lopinavir/ritonavir group, fewer patients in the atazanavir/ritonavir group had grade 2 to 4 treatment-related diarrhea (10 [2%] vs 50 [11%]) and nausea (17 [4%] vs 33 [8%]).

Grade 2 to 4 jaundice occurred in 16 (4%) of 441 patients in the atazanavir/ritonavir group but in none of 437 patients in the lopinavir/ritonavir group. There were grade 3 to 4 increases in total bilirubin levels in 146 (34%) of 435 patients in the atazanavir/ritonavir group and in 1 (< 1%) of 431 patients in the lopinavir/ritonavir group.

Limitations of this study include open-label design and use of 3 capsules twice daily of
lopinavir/ritonavir during the 48-week assessment period, rather than the newer tablet formulation of 2 tablets twice daily.

"In treatment-naive patients, atazanavir/ritonavir once-daily demonstrated similar antiviral efficacy to lopinavir/ritonavir twice-daily, with less gastrointestinal toxicity but with a higher rate of hyperbilirubinemia," the study authors write. "The results of this study support the use of once-daily atazanavir/ritonavir as a recommended first-line treatment option, with a number of patient benefits over the currently recommended ritonavir-boosted twice-daily lopinavir for the treatment of HIV-infected antiretroviral-naive patients."

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Clinical Context

Because of their potency and high genetic barrier to antiretroviral resistance, protease inhibitors remain a cornerstone of highly active antiretroviral therapy (HAART). The current international guidelines recommend ritonavir-boosted protease inhibitors, including lopinavir/ritonavir and atazanavir, as preferred, or alternative third-agent HIV medications for the start of HAART in antiretroviral-naive patients. Studies have demonstrated that atazanavir/ritonavir is as effective as lopinavir/ritonavir, with a more favorable lipid profile and less gastrointestinal toxicity in treatment-experienced patients with HIV-1 infection.

The aim of this study was to examine the comparative clinical efficacy of atazanavir/ritonavir and lopinavir/ritonavir directly in treatment-naive patients with HIV-1 infection.

Study Highlights

- In this open-label, international, noninferiority study, 883 antiretroviral-naive patients with HIV-1-infection were randomly assigned to receive atazanavir/ritonavir 300/100 mg once daily (n = 440) or lopinavir/ritonavir 400/100 mg twice daily (n = 443), in combination with fixed-dose tenofovir/emtricitabine 300/200 mg once daily between November 2005 through June 2006.
- Patients were eligible for enrollment if they were infected with HIV-1, aged 18 years or older, naive to antiretroviral therapy, and had HIV-1 RNA of 5000 copies per mL or greater.
- Baseline characteristics were similar between the 2 groups.
- The primary endpoint was the proportion of patients with viral load of less than 50 copies per mL at week 48. The main efficacy analysis was done by intent-to-treat.
- Secondary efficacy endpoints were the proportion of patients with HIV RNA of less than 400 copies at 48 weeks, change in CD4 cell count from baseline through 48 weeks, log reduction in HIV RNA by week 48, and the antiretroviral resistance profiles of patients experiencing virologic failure.
- Safety endpoints included the incidence of adverse events, serious adverse events, discontinuations because of adverse events, abnormal results on laboratory tests, and changes from baseline in laboratory tests with time.
- Results revealed that at week 48, there were 343 (78%) of 440 patients receiving atazanavir/ritonavir and 338 (76%) of 443 patients receiving lopinavir/ritonavir who had achieved a viral load of less than 50 copies per mL (difference, 1.7%; 95% CI, –3.8 to 7.1).
- Mean increases from baseline in CD4 cell count were similar (203 cells per µL in the atazanavir/ritonavir group vs 219 cells per µL in the lopinavir/ritonavir group).
- There were no differences between the 2 groups in log reduction in HIV RNA from baseline and week 48.
- By week 48, virologic failures occurred in 25 (6%) patients in the atazanavir/ritonavir group and in 26 (6%) in the lopinavir/ritonavir group.
- Only 2 patients (both in the atazanavir/ritonavir group) had nonpolymorphic protease-inhibitor–resistance mutations emerge on treatment, which conferred phenotypic resistance to atazanavir in 1 patient.
- Serious adverse events were noted in 51 (12%) of 441 patients in the atazanavir/ritonavir group and 42 (10%) of 437 patients in the lopinavir/ritonavir group. Fewer patients in the atazanavir/ritonavir group vs the lopinavir/ritonavir group experienced grade 2 to 4 treatment-related diarrhea (10 [2%] vs 50 [11%]) and nausea (17 [4%] vs 33 [8%]).
- However, grade 2 to 4 jaundice was seen in 16 (4%) of 441 patients in the atazanavir/ritonavir group vs none of 437 patients in the lopinavir/ritonavir group; grade 3 to 4 increases in total bilirubin levels were seen in 146 (34%) of 435 patients receiving atazanavir/ritonavir and in 1 (< 1%) of 431 patients receiving lopinavir/ritonavir.
- Only 3 patients (< 1%) discontinued treatment with atazanavir/ritonavir because of jaundice within the 48 weeks.
- Mean percentage changes in fasting total cholesterol, non–high-density lipoprotein
cholesterol, and triglyceride levels from baseline at week 48 were significantly higher in patients receiving lopinavir/ritonavir vs patients receiving atazanavir/ritonavir (P < .0001). More patients receiving lopinavir/ritonavir vs those receiving atazanavir/ritonavir used lipid-lowering therapy.

**Pearls for Practice**

- Compared with lopinavir/ritonavir, atazanavir/ritonavir has a more favorable lipid profile and less gastrointestinal toxicity in treatment-experienced patients with HIV-1 infection.
- In treatment-naive patients, atazanavir/ritonavir once daily demonstrated similar antiviral efficacy to lopinavir/ritonavir twice daily, with less gastrointestinal toxicity and more favorable lipid profile but with a higher rate of hyperbilirubinemia.

**CME Test**

Compared with lopinavir/ritonavir, atazanavir/ritonavir may be preferred in all of the following patients except:

- Younger patients
- Patients with chronic diarrhea
- Patients with previous myocardial infarction
- Patients with issues of dosing compliance

According to the study by Molina and colleagues, which of the following statements is not correct regarding atazanavir/ritonavir and lopinavir/ritonavir?

- Atazanavir/ritonavir once daily demonstrated similar antiviral efficacy to lopinavir/ritonavir twice daily
- Mean increases from baseline in CD4 cell count were similar in the atazanavir/ritonavir group vs the lopinavir/ritonavir group
- Grade 2 to 4 jaundice was seen in more patients in the atazanavir/ritonavir group, but grade 3 to 4 increases in total bilirubin levels were observed more in the lopinavir/ritonavir group
- Mean percentage changes in fasting total cholesterol, non–high-density lipoprotein cholesterol, and triglyceride levels from baseline were significantly higher in patients receiving lopinavir/ritonavir vs patients receiving atazanavir/ritonavir

**Save and Proceed**