A second study confirms fat loss issues with efavirenz

In the mid-1990s, long before the use of double protease inhibitors (PIs) was recommended, researchers at the Ottawa General Hospital were leaders in experimenting with the use of ritonavir-boosted PI combinations. So, it should come as no surprise that researchers at that hospital are once again conducting studies with boosted PIs.

Because HAART often involves taking many pills and has both short-term and long-term side effects, researchers are trying to find ways to minimize the burden of pill-taking and reduce side effects. A strategy that might be tested is to first suppress HIV replication as low as possible, and then to switch PHAs to a less intensive regimen. This is called induction-maintenance.

Lopinavir/r (Kaletra) is a potent protease inhibitor that is commonly used as part of HAART. Recently, Canadian researchers as well as others in France, Spain, the UK and the US collaborated in a study to assess the effectiveness of one induction-maintenance strategy:

- Starting therapy with lopinavir/r + 2 nukes and then eventually switching some participants (those whose viral loads were below the 50-copy mark for three consecutive months) to a less intensive therapy for several years— lopinavir/r alone (Kaletra monotherapy). As a comparison, a group of similar PHAs would be kept on a regimen of efavirenz + 2 nukes also for two years.

**Study details**

Researchers recruited 106 participants—74 were assigned to receive lopinavir/r + 2 nukes and 32 were to receive efavirenz + 2 nukes. No PHAs in this study had previously used anti-HIV therapy.

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

- 22% female, 78% male
- age – 38 years
- CD4+ count – 230 cells
- viral load – about 100,000 copies

Low-dose X-ray scans called DEXA, taken every six months, were used to assess changes in body fat.

After the third month of the study, participants who were receiving lopinavir/r + 2 nukes had their viral load assessed every month. Those participants whose viral load was below the 50-copy mark for three consecutive months then discontinued AZT and 3TC starting in the sixth month of the study and used only lopinavir/r (Kaletra monotherapy).

**Results**

In this report we will focus on the side effects related to the use of therapies in this study. In a separate report we will cover issues related to antiviral activity and resistance. In general, the antiviral effect of each regimen was found to be roughly equivalent.

**Results—Changes in body shape**

Initially, both groups experienced increased limb fat as the adverse changes to the body caused by HIV were reversed with treatment. However, after the sixth month, limb fat levels in the efavirenz group began to decline. After one year, limb fat levels in the efavirenz group declined precipitously, falling well below their pre-study levels. Overall, the difference in limb fat between the lopinavir/r and efavirenz groups two years into the study was great—about 2 kilograms. Although low-dose X-ray scans were used to assess changes in body fat, it became obvious just by looking at participants exactly who was experiencing the loss of subcutaneous fat.

Researchers found that an increase in trunk fat (a gain of at least 20% from pre-study values) was linked to low
CD4+ cell counts. Those participants with low CD4+ counts at the start of the study were more likely to experience increased fat deposits in the belly.

Changes in lipid levels were generally not significant between groups, although there was a trend for slightly higher triglycerides among lopinavir/r users.

**REFERENCE:**

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Production of this content has been made possible through a financial contribution from the Public Health Agency of Canada.

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