Studied as a way to reduce excess deep belly fat, the synthetichuman growth hormone releasing factor called tesamorelin (Egrifta) was approved by the FDA in November 2010 and has been available since January 2011. Results from a 52-week study of 816 people showed 18% less deep belly fat in those on tesamorelin than those taking placebo. Although it may help some people trim down some of their deep belly or visceral fat (fat found under the stomach muscles), it should not be viewed as a weight control product. In HIV-positive people this visceral fat has been shown to increase a person’s risk for heart disease, though study results do not show a lowered risk of heart disease from using the drug. Tesamorelin does not affect subcutaneous fat, or the fat that’s found above the stomach muscles but below the skin.

Body shape changes
Many people with HIV, about 1 in 4, face a condition called lipodystrophy. The syndrome is due to several causes that can overlap and are not well distinguished by research. How to treat the condition can also become a complex set of decisions made you and your doctor.

The symptoms of lipodystrophy can vary from person to person. Some have fat loss, usually in the face, arms or legs (lipoatrophy). Others have fat gain, particularly on the neck or around the breasts or abdomen (lipohypertrophy). These visible symptoms can be accompanied by higher levels of blood fats (dyslipidemia) and by changes in insulin or blood sugar (hyperglycemia).

One common symptom, excess deep belly fat, can be troublesome. Not only do many feel uncomfortable and conspicuous with a larger belly, it can also prove painful to some or restrict others from being as active as they once were. This visceral fat lies beneath the stomach muscles near the internal organs, increasing the risk for heart disease. The condition can result from genetic factors, diet, HIV-related drugs and from HIV itself.

Study volunteers
In a Phase 3 study, 550 people were given 2mg tesamorelin while 266 were given placebo, by injection into the stomach once a day. Adherence to the regimen was 99% or higher for both groups. All had CD4s above 300, and 3 out of 4 had undetectable viral loads. Average time on HIV therapy was 4.5 years, average time since diagnosis of visceral fat was 4 years, and average age was 48. Average waist size was 41 inches.

The average time living with HIV since diagnosis was about 13 years. More than 4 out of 5 were men. Study volunteers used several different HIV regimens: NNRTIs + NRTIs (33%), protease inhibitors + NRTIs (45%), NNRTIs + NRTIs + protease inhibitors (10%), NRTIs only (5%), or other regimens (7%).

Study design
The goal of the study was to assess how much fat loss would occur from using tesamorelin compared to placebo (first 26 weeks). For the second 26 weeks, everyone on placebo was given tesamorelin while those who had already taken the drug were then divided to continue on it or start taking...
Tesamorelin and excess deep belly fat

placebo. Body scans were taken before starting therapy, during the study, and at 52 weeks. Other tests were also taken, such as those for cholesterol, triglycerides, glucose, insulin and belly image.

**Side effects**
Side effects were similar between the two groups, though more volunteers quit the tesamorelin group than those on placebo. Injection site redness and itchiness were common (about 1 in 4). Joint pain and general aches and pains were also noted as well as fluid retention.

Increased markers for diabetes occurred about 3.5 times more often in people on tesamorelin. Therefore, people should be checked regularly for possible diabetic conditions. As well, allergic skin rashes occurred in about 4% of people on the drug which may need prompt medical care.

One concern from using tesamorelin is the build-up of antibodies to it in some people. Nearly all those with skin reactions tested positive for these antibodies. Their significance is unknown at this time, but the concern is that they could reduce the effects of the drug over time. During this study, these antibodies didn’t appear to “neutralize” in this way, but more follow-up needs to be done.

**Study results**
At 26 weeks, tesamorelin reduced deep belly fat by 13% compared to placebo. At 52 weeks, for those who continued on the drug, tesamorelin reduced it by nearly 18%. Those who took tesamorelin for 26 weeks and then placebo for 26 weeks showed a reverse in symptoms, with gaining the deep belly fat back rather quickly within about three months.

Tesamorelin did not significantly change cholesterol levels. However, it did reduce triglycerides, which help lower the risk for heart disease. It also increased insulin-like growth factor (IGF-1), which may promote the growth of tumors.

People who were on regimens of NRTIs + protease inhibitors or NRTIs-only had slightly higher rates of visceral fat loss. Another possible benefit from using tesamorelin appears to be a small increase in lean body mass, but nowhere near the levels seen with the human growth hormone called Serostim.

As for the self-assessment, the data are still positive though not as convincing. Three scores were checked at the start and end of the study: the level of distress a person felt by his/her belly image, the doctor’s judgment of the change in belly fat, and the person’s opinion of that same change.

Volunteers generally felt better about their belly image after using tesamorelin compared to placebo, though it was only slightly better. Similarly, doctors believed there was some improvement in fat loss. However, many people using tesamorelin did not notice a change in the size of their bellies or waists.

**Who should not use tesamorelin?**
Given the potential for developing cancer when using tesamorelin, individuals should be screened and assessed for current or possible new cancers. People should weigh the risks and benefits before making decisions to start on the drug. Tesamorelin has not been studied in children.

Pregnant women and people with an active cancer should not use it. People going through cancer treatment should wait until their therapy has stopped and it’s clear that the cancer has become inactive before starting tesamorelin. Also, anyone with earlier head trauma, radiation of the head, or issues regarding the pituitary gland should not use the drug.

Since clinical study beyond a year has not been done, it’s unknown what long-term side effects may occur, including heart health. In people who start tesamorelin but do not show clear improvement in their deep belly fat and longer-term use may be questionable, it may be wise to stop using the drug.
How to get tesamorelin?
The distribution of tesamorelin will be tightly controlled by prescriptions through the EMD Serono Axis Center at 877-714-2947 (fax 866-823-9554). The program is now open for new prescriptions. The Patient Assistance Program will cover people at 600% FPL (Federal Poverty Level).

A Co-pay Assistance Program is also available for people with a valid prescription and insurance that covers the drug. People who use Medicaid, Medicare or other public programs cannot use the card. The first use must be made before December 31, 2011, and can be used for up to $200/month savings and up to 12 times before December 31, 2012. Ask your doctor or call the Axis Center for the co-pay card.

How to take tesamorelin?
The drug is given as a shot once a day under the skin in the area below the belly button. Two vials of drug must be mixed with sterile water before injection. The drug must be mixed just before using, which may make it difficult for some people to take on time every day. Since many people are inexperienced in giving themselves a shot every day, the drug company offers everyone a one-on-one training with an “injection trainer” who can show the mixing and injection process. Used needles should be kept in a sharps container and properly disposed of.

Project Inform’s Perspective
The reasons why a person wants to use tesamorelin may be more of a deciding factor in treating deep belly fat. While it may get rid of some visceral fat, the modest reduction may not be enough to feel better about one's belly size. However, getting rid of some of this fat may be enough to ease the discomfort that some people face with excess deep belly fat.

Tesamorelin appears to increase a certain insulin level which may lead to diabetes in some people, especially those with a pre-diabetic condition. As well, the drug may promote the growth of tumors, but longer-term follow-up is needed.

It’s unknown how much more benefit, such as further fat loss, or even what side effects can occur from using it for more than a year, such as the appearance of tesamorelin antibodies. Also, its cost is high and may be available to only those with certain insurance plans.

More study is needed to see if various doses of tesamorelin could achieve the same (or better) results, including cycling on and off the drug. This could reduce the number of injections over time. For now, to keep the visceral fat from coming back, people are faced with injecting themselves every day, which some are not willing or able to do.

Complete prescribing information is available at www.emdserono.com.