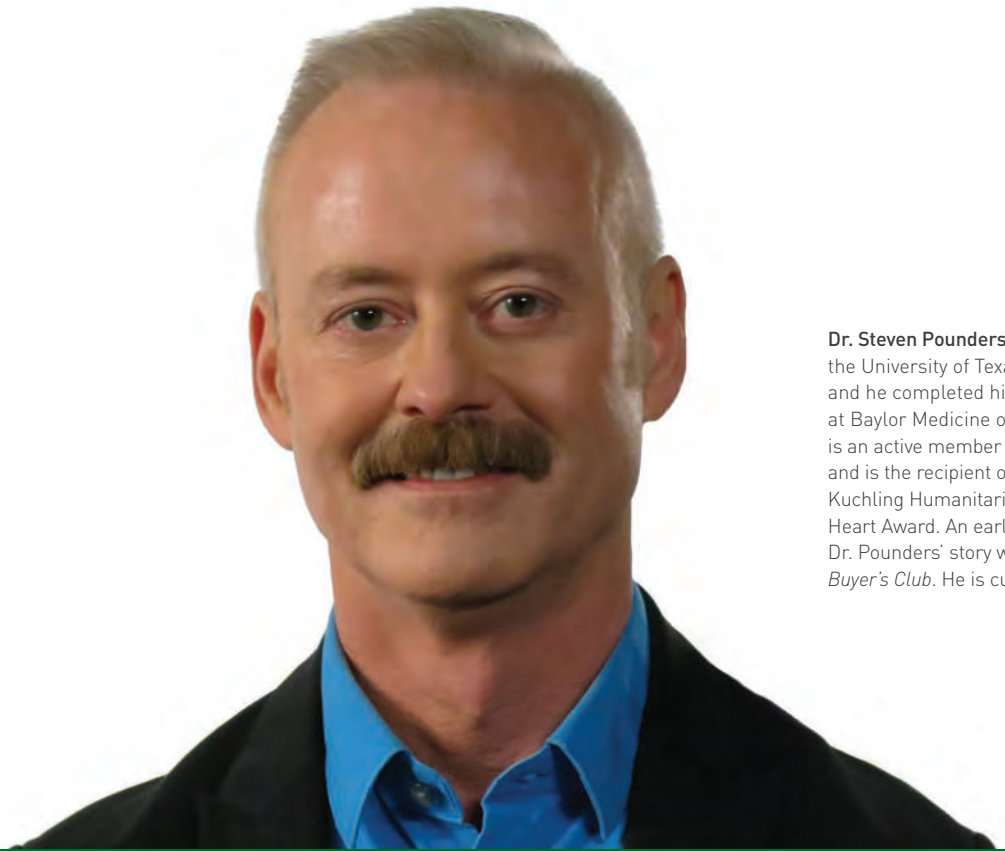

Dr. Steven Pounders received his medical degree from the University of Texas Medical Branch at Galveston, and he completed his residency in internal medicine at Baylor Medicine of College in Houston. Dr. Pounders is an active member of the HIV education community and is the recipient of several honors, including the 2017 Kuchling Humanitarian Award and the 2014 CURE Open Heart Award. An early advocate for patients with HIV, Dr. Pounders' story was featured in the movie *Dallas Buyer's Club*. He is currently in private practice in Dallas.

Clinical Conversations in HIV-Associated Wasting

A brief discussion with Steven Pounders, MD

INDICATIONS AND USAGE

Serostim® (somatropin) for injection is indicated for the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance. Concomitant antiretroviral therapy is necessary.

IMPORTANT RISK INFORMATION

CONTRAINDICATIONS

Serostim® should not be used in patients with acute critical illness, active malignancy, hypersensitivity to somatropin or any of its excipients, or diabetic retinopathy. Increased mortality has been reported in patients with acute critical illness due to complications following surgery, multiple accidental trauma, or acute respiratory failure. Preexisting malignancies should be inactive and treatment completed prior to instituting therapy. Serostim® should be discontinued if there is evidence of tumor recurrence. Systemic hypersensitivity reactions have been reported with postmarketing use of somatropin products.

Please see additional Important Risk Information throughout and enclosed Full Prescribing Information.

Serostim®
(somatropin) for injection

A brief discussion with Steven Pounders, MD

Q: Your work in caring for people living with HIV began before HAART was introduced. Can you tell us how the field of HIV care has changed over the past several decades?

A: My early years of working in HIV were intense. Patients were dying every week. Then HAART came around and suddenly things started to change. Treatments were better tolerated, and today medications have become even less toxic. As most of our patients living with HIV are doing so well with HAART, it does feel that problems with complications stemming from HIV have diminished. However, because some have fortunately survived for as long as they have, we still see HIV-related problems. We also see more of our patients getting chronic diseases, just like the rest of the population.

Q: How often do you see HIV-associated wasting among patients in your practice?

A: More than 90% of our patients have undetectable viral loads. While many of my patients struggle to lose weight, as does much of the general US population, I do have patients who need to gain the weight they have lost without trying. We have learned that with HIV, there are attacks on the lining in the gut very early on, which may cause problems with their immune systems and immune activation. This results in increased inflammation and activation, which interferes with nutrient absorption, resulting in loss of lean body mass and body weight.

Q: How do you think HIV-associated wasting is viewed today?

A: In our society so many people are overweight. People who lose weight unintentionally don't get a lot of sympathy from others. Most people think "Thin is in, thin is good." But for those with HIV-associated wasting, it places them at a higher risk for morbidity and mortality. When you are HIV-positive, a lower body mass index is not ideal. A person can even have a normal BMI, but it may be declining due to a loss of weight that is unexpected or unplanned. That is why we cannot rely only on BMI to determine wasting. We need to monitor any decrease in weight or BMI and really listen to patient concerns over time to ensure that we do not miss wasting syndrome.

To those who believe that wasting no longer exists, I would remind them that it continues to impact a range of patients both male and female. In fact, I diagnose patients with it on a regular basis. These include patients who have immune reconstitution, as defined by increasing T cells, and those with have undetectable viral loads. It also includes those who are recently diagnosed with HIV or living with HIV for many years, those who seem to tolerate their medications very well, and those who have no evidence of infections or are recovering from an acute infection.

Q: How do you diagnose HIV-associated wasting?

A: One of the first steps I take, especially in men, is to check their hormone profile. Then we look for vitamin deficiencies that can be corrected. They see a dietitian to ensure that their appetite is good and that they are getting the nutrition they need, and if warranted, we will try appetite stimulants or anabolic agents. We also screen for active infections. We certainly want to get them therapeutically corrected if they are deficient in testosterone or other hormones. Even when we address all these factors, some patients do not regain the weight they have lost or they are still losing weight and lean body mass and have decreased energy for no apparent reason.

Q: What else do you look for?

A: I routinely ask general questions about fatigue and their daily routines. Are they able to do regular exercises? At first, some patients will only mention that they experience fatigue—fatigue meaning they can barely make it through the day. They cannot get their work done and they are not doing extracurricular activities or their regular exercise routines. Patients don't want to complain because they don't realize it can be fixed. They say, "Oh, my T cells are good. My viral load is down. I'm doing great." But they're not doing great.

If the physician doesn't know the patient is experiencing symptoms of HIV-associated wasting, he or she can't treat it. That's why it's important that we ask probing questions during visits.

Q: Can you tell us about a patient you've treated with Serostim® (somatropin) for injection?

A: My patient was a 40-year-old white male with a CD4-cell count of 410-640 cells/mm^3 and an RNA viral load of 20 copies/mL. He began to develop problems with his memory and cognition. He could no longer work and had HIV-associated neurocognitive disorder.

Despite a head CT scan, MRI, and lumbar puncture, we found nothing but HIV. Then in the next year, he started to lose weight and became very fatigued. We checked all of the markers I recommended earlier. He needed testosterone, anabolics, and appetite stimulants. Over the next few months, he continued to lose weight and I was really getting more concerned about him. He used go to the gym regularly and lift weights, and he was not able to do that any longer.

After excluding other reasons for weight loss, I started him on Serostim®. I saw him start to gain weight and gain some energy. He could go back to the gym and work out slowly and progressively. I still see him, and he is doing really well.

Q: In general, how are patients affected by Serostim® therapy?

A: When you face a life-threatening illness such as HIV, it is important to watch for a 5% or more loss of body weight because it does portend a poor prognostic signal. That's why it's important to get appropriate patients started on treatment with Serostim® and help them to understand how helpful it can be.

We are fortunate to have treatments like testosterone, nutritional supplements, and other options to help temporize and help improve the patient. With Serostim® we have been able to change the course of wasting in people living with HIV. When I see unexplained weight loss and decreased lean body mass and energy in a patient, I always consider the need to prescribe it.

IMPORTANT RISK INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS

Acute Critical Illness: Increased mortality in patients with acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure has been reported after treatment with [pharmacologic amounts of] somatropin.

Patient Case

Clinician's observation: "We need to monitor any decrease in weight or BMI and really listen to patient concerns over time."

PATIENT PROFILE

40-year-old male diagnosed with HIV in 2006. Despite adherence to antiretrovirals, patient experienced progressive fatigue and weight loss, ultimately causing him to leave his job. An extensive workup was completed. The patient was initiated on several treatments: testosterone to address hypogonadism, and anabolics and appetite stimulants to counteract weight loss. He continued to lose weight and express concerns about fatigue. At that time, Serostim® (somatropin) for injection was initiated for HIV-associated wasting.

RELEVANT MEDICAL HISTORY

- HIV+ (2006)
- HIV-associated neurocognitive disorder

SOCIAL HISTORY

- Exercised regularly prior to reports of fatigue and weight loss
- Employed prior to reports of fatigue and weight loss
- Reports no illicit drug use

WEIGHT HISTORY

- Height: 5'8"
- Premorbid weight: 146 lb
- Premorbid BMI: 22.2
- Weight at HIV-associated wasting diagnosis: 130 lb
- BMI at HIV-associated wasting diagnosis: 19.8

OVERVIEW OF SYMPTOMS AT TIME OF HIV-ASSOCIATED WASTING DIAGNOSIS

- Decreased physical endurance; no longer able to complete usual exercise routine
- Fatigue
- Poor appetite
- Unintentional weight loss

LABORATORY AND IMAGING RESULTS

- CD4-cell count: 410-640 cells/mm^3
- Viral load: Less than 20 copies/mL
- Testosterone levels: Below normal range
- CT scan, MRI, and lumbar puncture: Normal
- No vitamin deficiencies

TREATMENT HISTORY

- Anabolic steroids
- Appetite stimulants
- Testosterone replacement therapy

This case study represents a real patient of Dr. Pounders, however, it may not be a complete representation of the individual's entire medical case or include his full experience with Serostim®. Certain details such as concomitant medications, dose adjustments, and adverse reactions may not be reflected. For more information obtained from clinical trials and unsolicited post-marketing reporting of adverse experiences, refer to the Important Risk Information throughout and see enclosed Full Prescribing Information.

IMPORTANT RISK INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

Concomitant Antiretroviral Therapy: Somatropin has been shown to potentiate HIV replication in vitro, however there was no increase in virus production when antiretroviral agents were added to the culture medium. All patients received antiretroviral therapy for the duration of treatment during Serostim® clinical trials and no significant increase in viral burden was observed.

Neoplasms: Patients with preexisting tumors should be monitored for progression or reoccurrence. Monitor patients on somatropin therapy carefully for preexisting nevi.

Please see additional Important Risk Information continued on the back and enclosed Full Prescribing Information.

Help your patients with HIV-associated wasting keep moving forward with Serostim® (somatropin) for injection

Serostim® is the only FDA-approved treatment to increase lean body mass and weight as well as improve physical endurance—3 key elements of HIV-associated wasting.

In clinical trials, after 12 weeks of treatment with Serostim®, patients with HIV-associated wasting experienced statistically significant increases in lean body mass and weight and clinically and statistically significant improvements in physical endurance.

IMPORTANT RISK INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

Impaired Glucose Tolerance/Diabetes: Cases of new onset impaired glucose tolerance, new onset type 2 diabetes, and exacerbation of preexisting diabetes have been reported in patients receiving Serostim®. Some patients developed diabetic ketoacidosis and diabetic coma. Patients with risk factors for hyperglycemia and glucose intolerance should be monitored closely and those using antidiabetic agents may require dose adjustment.

Intracranial Hypertension: Intracranial hypertension (IH) with papilledema, visual changes, headache, nausea, and/or vomiting has been reported. Funduscopic examination should be performed prior to initiating treatment with Serostim® and periodically during the course of treatment. If papilledema is observed, treatment should be stopped and restarted at a lower dose after IH-associated symptoms have resolved.

Severe Hypersensitivity: Serious systemic hypersensitivity reactions including anaphylactic reactions and angioedema have been reported with postmarketing use of somatropin products. Patients and caregivers should be informed that such reactions are possible and that prompt medical attention should be sought if an allergic reaction occurs.

Fluid Retention/Carpal Tunnel Syndrome: Swelling (particularly in the hands and feet), musculoskeletal discomfort, or carpal tunnel syndrome may occur during treatment with Serostim®. Symptoms may resolve spontaneously, with analgesic therapy, or after reducing the frequency of dosing. If symptoms of carpal tunnel do not resolve by decreasing the weekly number of doses, it is recommended that Serostim® treatment be discontinued.

Skin Atrophy: Rotate the injection site to avoid tissue atrophy.

Pancreatitis: Cases of pancreatitis have been reported rarely. Consider pancreatitis in patients who develop persistent severe abdominal pain.

ADVERSE REACTIONS

In clinical trials in HIV-associated wasting or cachexia the most common adverse reactions (incidence >10%) were increased tissue turgor, arthralgia, myalgia, and arthrosis, which may be responsive to dose reduction. Other common adverse reactions (incidence >5%) included nausea, fatigue, gynecomastia, paresthesia, generalized edema and hypoesthesia.

SPECIAL POPULATIONS:

Somatropin should be used during pregnancy only if clearly needed and with caution in nursing mothers because it is not known whether somatropin is excreted in human milk. The safety and effectiveness of somatropin in patients with hepatic or renal impairment or in patients aged 65 years and over have not been evaluated in clinical studies.

Please see the enclosed Prescribing Information for full disclosure.

EMD SERONO

Serostim®
(somatropin) for injection