

SLIT vs SCIT: A Q&A

By Pippa Wysong

Sublingual immunotherapy (SLIT) is gaining acceptance in otolaryngology circles, but is it really any better than subcutaneous injections? Which patients can benefit from it? How can it affect practice?

These are questions *ENTToday* set out to answer by asking three physicians who use SLIT in practice: Bradley F. Marple, MD, Professor of Otolaryngology at University of Texas Southwestern Medical School; Mary Morris, MD, an allergist and partner at Allergy Associates of La Crosse, and Medical Director for Allergy Choices in Wisconsin; and Steven B. Levine, MD, Assistant Clinical Professor of Otolaryngology at Yale University.

What is SLIT, and how is it used?

Dr. Levine: Sublingual immunotherapy (SLIT) is the application of FDA-approved antigens to the sublingual mucosa rather than injected as they are with traditional

subcutaneous immunotherapy (SCIT). It's the same concentration of antigen, and the same units of antigens per milliliter of solution. It's just the diluent that's different.

How does SLIT work? How does its mode of action differ from that of SCIT?

Dr. Morris: Once the antigens are placed under the tongue, it appears that dendritic cells take up the antigen, migrate to cervical lymphatic nodes, and have an effect on T-regulatory cells, which then cause a systemic response. It takes advantage of the mucosal immune system, which behaves differently from the humoral immune system.

Research has found that once the antigen drops are placed under the tongue, within 30 seconds those antigens are taken up by dendritic cells and go below the mucosal surface—where they're not washed



Once a patient decides on SLIT versus injection therapy, the first dose is administered in the office, but subsequent doses may be taken at home.

away. They remain there for about 18 to 20 hours while they start doing their job of sending the signals to the T-regulatory cells.

Dr. Marple: Some data suggest that the antigens remain within the tissues adjacent to the oral mucosa and only minimally gain access to the systemic circulation, and some suggest that antigen is retained within the local submucosal lymphatic tissue. Most data suggest that very little antigen migrates to the regional cervical lymph nodes.

What triggered the idea for this mode of delivery of antigens?

Dr. Morris: The idea really got going in Europe. Around 1986, injection IT was practically banned in England because of some deaths that were linked to the therapy. If you were going to get injection-based immunotherapy it had to be in a hospital. This prompted people to start looking to see if there was a safer way of doing immunotherapy. Europe led the way in this, though my father, an allergy researcher, was one of the first people in the US to publish

something on SLIT, in 1969 and 1970.

Dr. Marple: In the US there was use of the sublingual approach by homeopaths, but the doses were quite low, and the studies relating to it weren't of high quality. The doses being used in Europe were much higher and approximated those that were being given by subcutaneous routes. Over the past decade, rigorous clinical trials have demonstrated that when delivered in adequate doses, this was a viable form of antigen delivery. Now, SLIT is becoming more mainstream in the US.

How effective is SLIT compared with SCIT? How do the safety profiles compare?

Dr. Marple: The efficacy from this different route of delivery for immunotherapy appears in most outcome studies to be roughly equivalent to subcutaneous IT. While some studies fail to show significant benefit, a recent Cochrane meta-analysis demonstrated efficacy in control of rhinitis

continued on page 18

SLIT vs SCIT*continued from page 16*

symptoms in patients older than 12 years. Further, there was a trend suggesting that better results were seen in studies that made use of higher doses of antigen, suggesting that total dose of antigen is important. Conversely, insufficient pediatric data were available to make an assessment. The huge difference is in the safety profile. This appears to be much safer than subcutaneous IT.

Are the same antigens used for SCIT and SLIT?

Dr. Levine: Yes. You have the same variety, and you can treat patients with a larger number of antigens using drops [SLIT] compared to the shots. With individual injections, there are limitations to what we normally mix together. For instance, some like to keep the mold antigens separate from the trees, grasses, and leaves. Others might want to keep dust separate from the animal antigens. And there is a limitation to how many injections patients will tolerate.



“I think that this is an outstanding alternative for patients who would otherwise not want to go through injection immunotherapy. They can avoid the needles and the inconvenience of having to come into the office as much.”

—Steven Levine, MD

Dr. Morris: A Scandinavian study compared the effectiveness and safety of injection therapy with SLIT using birch pollen antigens. It was a placebo-controlled, double-blind, double-dummy trial. Both therapies showed superiority over placebo, and statistically there was no difference between subcutaneous and sublingual in terms of efficacy. However, safety was markedly better with sublingual. It's the best-designed study we've had on this.

Many will limit it to four injections, plus limit the number of antigens in each one of these injections. This is all in an effort to reduce adverse reactions. However, with SLIT there are so few reactions, we can actually use more antigens simultaneously safely. Typically, in our practice, we'll mix as many as 20 antigens in a single bottle.

Does using SLIT require much training?

Dr. Marple: I would not like to lose sight of the fact that this is one component of the



“The knowledge needed is quite similar to what you need to know for subcutaneous injection; it's basically knowing how to mix up the treatment vials for the sublingual version.”

—Mary Morris, MD

overall management of allergic patients. Many otolaryngologists provide care for allergic patients, and manage them in their office. This is being taught in residency programs as mandated by ACGME. SLIT is one new tool in the overall management of allergic rhinitis, and is best incorporated into your practice after you've spent some time learning specifically about it. That being said, it's relatively straightforward and not overly difficult. Also, patients benefit from it.

Dr. Morris: The American Academy of Otolaryngic Allergy has a protocol and is teaching courses. Plus, courses are taught by private clinics and other associations. It shouldn't be difficult to find training. The knowledge needed is quite similar to what you need to know for subcutaneous injection; it's basically knowing how to mix up the treatment vials for the sublingual version.

How are patients selected for SLIT versus traditional IT?

Dr. Levine: Doctors should continue with the gold standard, which is injection therapy. At the same time, what I can tell you from my clinical experience of having done

this now for about six years, is I think that this is an outstanding alternative for patients who would otherwise not want to go through injection immunotherapy. They can avoid the needles and the inconvenience of having to come into the office as much.

Dr. Marple: The overarching questions are: Does SLIT replace SCIT, does SLIT augment traditional treatment, or does it provide another option? We don't yet have enough data to really differentiate which patients would really benefit from SCIT and who would be best served with SLIT. With my own patients, I inform them about each method of delivery. Then, I let the patients make the choice. Given a choice that is completely independent of reimbursement, I find patients almost uniformly prefer to go with SLIT.

How do you go about using SLIT?

Dr. Levine: In our practice, once the patient decides to use SLIT, we give the first dose in the office to make sure there's no reaction. Then we give them enough solution for 12 weeks at a time. If they're local, they stop in once every 12 weeks as we escalate the concentration of antigen and monitor their response. If they're patients who are traveling long distances, we ship drops to them and have them stop in and see us when it's convenient.

How does the off-label status affect the use of SLIT?

Dr. Marple: In reality, many treatments are used off-label. In otolaryngology, we're forced on a very regular basis to treat diseases “off-label.” Consider chronic rhinosinusitis; there are no FDA-approved medical therapies available to physicians. Practitioners must resort to the “off-label” use of a variety of medications such as antibiotics, antifungals, and corticosteroids. It's important to realize that all these medications have been approved for other uses by the FDA. Similarly, with SLIT, this is an off-label use of an already FDA-approved product.

Dr. Levine: Because it's not being used in the way that was originally approved by the FDA, we call it “off-label.” But should that limit us from offering SLIT to our patients? Absolutely not. Twenty percent of the drugs that are prescribed in the United States today are off-label FDA drugs. 