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Review

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# The KAAACI Guidelines for Sublingual Immunotherapy

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## ABSTRACT

Allergen immunotherapy is regarded as the only disease-modifying treatment option for various allergic conditions, including allergic rhinitis and asthma. Among the routes of administration of allergens, sublingual immunotherapy (SLIT) has gained clinical

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interest recently, and the prescription of SLIT is increasing among patients with allergies. After 30 years of SLIT use, numerous pieces of evidence supporting its efficacy, safety, and mechanism allows SLIT to be considered as an alternative option to subcutaneous immunotherapy. Based on the progressive development of SLIT, the current guideline from the Korean Academy of Asthma, Allergy, and Clinical Immunology aims to provide an expert opinion by allergy, pediatrics, and otorhinolaryngology specialists with an extensive literature review. This guideline addresses the use of SLIT, including 1) mechanisms of action, 2) appropriate patient selection for SLIT, 3) the currently available SLIT products in Korea, and 4) updated information on its efficacy and safety. This guideline will facilitate a better understanding of practical considerations for SLIT.

**Keywords:** Allergen immunotherapy; guideline; sublingual immunotherapy

## INTRODUCTION

Allergen immunotherapy (AIT) is a treatment that gradually increases the dose of causative allergens administered to allergic patients, ultimately creating tolerance to the allergen and reducing or eliminating the symptoms of allergic diseases including allergic rhinitis (AR).[1] It was first introduced by Noon[2] in 1911 to treat pollen-induced AR in patients, and has been used for the past 100 years or more.[3] AIT is the only treatment capable of curing allergic diseases.

The therapeutic effects of AIT have been verified in asthma, AR, and bee venom allergies, and recently, it has been introduced to treat atopic dermatitis and food allergies.[1] In addition to the traditional administration method of subcutaneous immunotherapy (SCIT), the safer and simpler method of sublingual immunotherapy (SLIT) has been widely used for the past 30 years, and additional methods such as oral immunotherapy, epicutaneous immunotherapy, and intralymphatic immunotherapy have been developed.

The working group on AIT and allergen from the Korean Academy of Asthma, Allergy and Clinical Immunology presented the principles and methods of AIT in 2010.[4] Hence, the working group updates the AIT guideline with an extensive review of literature, dealing with various topics such as the mechanism, indication, administration, clinical efficacy, adverse events, optimal treatment duration, and long-term efficacy of AIT. Here, we provide clinical practice guidelines for SLIT based on expert opinions by specialists in allergy, pediatrics, and otorhinolaryngology. The quality of evidence was rated according to the GRADE approach.[5] Each chapter begins with a summary that highlights the key points and provides the level of evidence.

## MECHANISM

### Summary statement

1. The primary principle of AIT is induction of allergen-specific peripheral tolerance and maintenance of the long-term unresponsiveness to allergens (high).
2. During AIT, increases in the production of regulatory T cells, inhibitory cytokines, such as interleukin (IL)-10, and decreased allergen-specific immunoglobulin E (sIgE), in addition to boosted allergen-specific IgG4 (sIgG4) production, are induced within weeks of starting AIT. This inhibits the production of dendritic cells, T cells, mast cells, basophils,

and eosinophils and reduces early and late inflammatory responses in tissues (high).
3. The oral mucosa is a site of intense immune activity and immune privilege, or tolerance is known to exist in the oral mucosa (high).

The mechanism of AIT has not yet been clearly elucidated. Summarizing previous studies, the mechanisms of immune responses to SCIT and SLIT are similar, but they do not induce the identical changes. In addition to most of the systemic immune responses shown in SCIT, additional local immune mechanisms, such as those of the oral mucosa and lymph nodes, may play an important role in SLIT. An important mechanism in AIT is to induce allergen-specific peripheral tolerance of the peripheral organs. During this process, T cells (mainly Foxp3+ natural regulatory T cells and inducible regulatory T cells) and B cells play important roles.[6] By inducing Treg cells, the production of sIgE is suppressed while the production of sIgG4 is induced, and inhibiting the production of dendritic cells, T cells, mast cells, basophils, and eosinophils reduces early and late inflammatory responses in tissues (**Figure**).[7,8]

In the case of SLIT, the tablet is placed under the tongue for about 1–3 minutes before swallowing so that the antigen can be absorbed through the sublingual mucosa. The dendritic cells involved in SLIT are myeloid dendritic and Langerhans cells. Dendritic cells can rapidly detect allergens that have entered through the sublingual mucosa and produce IL-10, IL-12, and transforming growth factor (TGF)-β. They reduce the Th1 immune response through IL-12, IL-10, and IL-27 secreted from dendritic cells, and the Th2 immune response

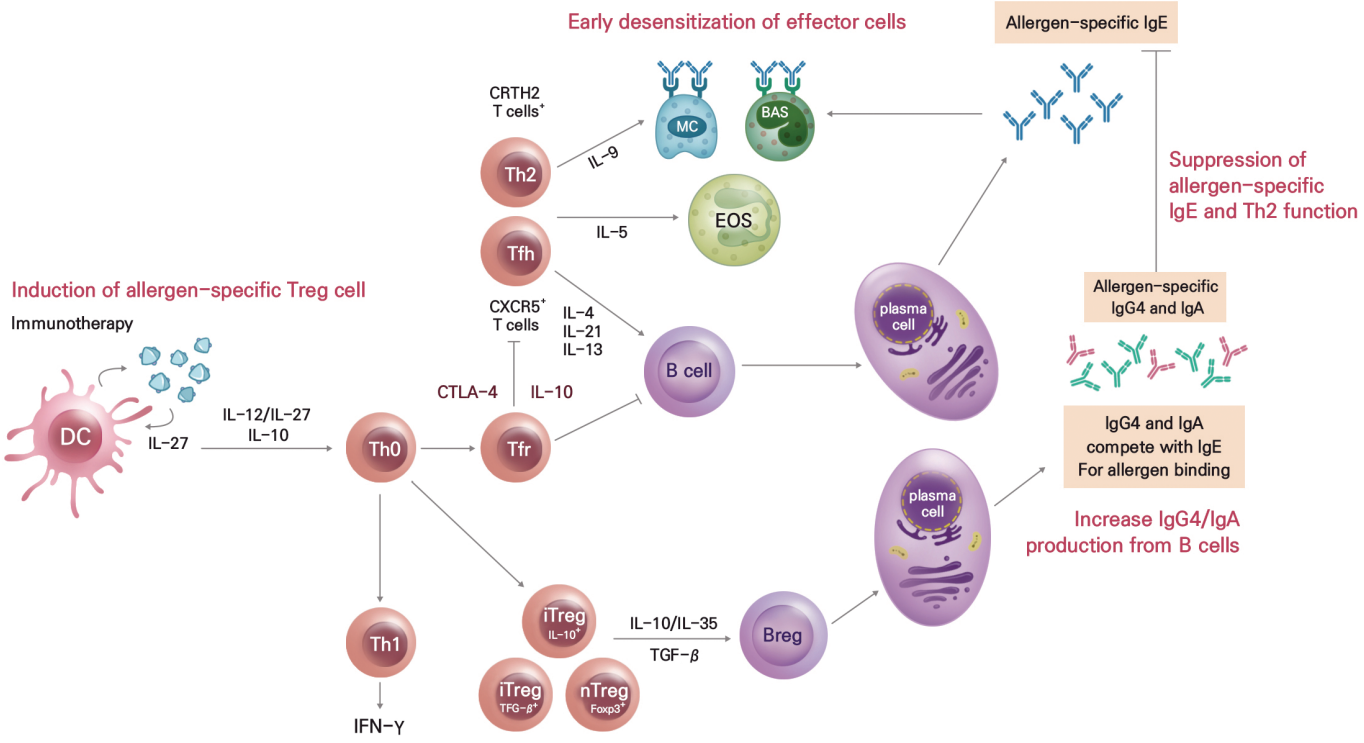


**Figure.** Mechanisms of allergen immunotherapy.
This figure is reproduced with permission: "Lee HY, Lee SM, Kang SY, Kim K, Kim JH, Ryu G, et al. KAAACI Guidelines for Allergen Immunotherapy. Allergy Asthma Immunol Res 2023;15:725-56."[8]
Treg, regulatory T; DC, dendritic cell; IL, interleukin; Th, T helper; IFN, Interferon; CRTH2, chemoattractant receptor homologous with T-helper cell type 2 cells; Tfh, follicular helper T; CXCR5, C-X-C chemokine receptor 5; CTLA-4, cytotoxic T lymphocyte-associated antigen 4; Tfr, follicular regulatory T; iTreg, inducible regulatory T; nTreg, natural regulatory T; TGF, transforming growth factor; Foxp3, forkhead box P3; MC, mast cell; BAS, basophil; EOS, eosinophil; Breg, regulatory B; Ig, immunoglobulin.


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by activating the Th3 immune response through TGF-β and IL-10, in addition to activating an IgA-mediated humoral immune response through TGF-β.[9,11]

Unlike SCIT, SLIT is not systematically administered into the vascular system, so systemic side effects such as anaphylaxis are less likely to occur, and the administered antigen is less likely to be detected in the blood.[6] Since the immune response in SLIT depends on the relatively fixed number of dendritic cells present in the sublingual mucosa, the extent is inevitably limited compared to that by the systemic immune response. However, many studies have reported that once the effective dose is reached, increasing the dose does not lead to an enhanced effect.[12,13]

## INDICATIONS AND CONTRAINDICATIONS

### Summary statement

1. AIT should be considered in patients with AR who have symptoms induced by the relevant allergen exposure and show evidence of clinically relevant sIgE (skin prick test and/or serum sIgE) (high).
2. SLIT is considered for patients with moderate/severe AR who 1) are not controlled with allergen avoidance and/or pharmacotherapy, 2) wish to receive AIT to avoid the adverse effects, costs, or long-term use of pharmacotherapy, 3) desire the potential benefit of AIT (e.g., prevention of asthma development or new sensitization), or 4) do not want to continue SCIT because of systemic side effects during its administration (high).
3. Absolute contraindications to AIT include uncontrolled or severe asthma, current/active malignant diseases, active systemic autoimmune diseases, or initiation during pregnancy (high).

As with SCIT, patients with persistent and severe AR may be indicated for SLIT if sIgE associated with clinical symptoms is detected through an allergy skin test or serological test.[14] SLIT is considered for 1) patients whose symptoms are not adequately controlled by conventional pharmacotherapy, such as H1-antihistamines or topical medications, 2) patients who show side effects of pharmacotherapy, 3) patients who want to reduce or avoid long-term pharmacotherapy, 4) patients who do not want to continue SCIT because they experienced systemic side effects during administration, and 5) patients who have shown low compliance with SCIT, including resistance to injection therapy.[14-17] The efficacy of SLIT has been demonstrated in adults as well as children and adolescents.[18-21] No minimum age at which SLIT can be initiated has been defined, and age was shown not to be a major limitation, when based on data on the safety of SLIT in infants.

Absolute contraindications to AIT (both SCIT and SLIT) are 1) uncontrolled or severe asthma, 2) patients with current/active malignant diseases, or 3) those with active systemic autoimmune diseases. Relative contraindications are 1) patients on long-term use of β-blockers or angiotensin-converting enzyme inhibitors because of hypertension, coronary artery disease, and other conditions (i.e., those who cannot use epinephrine in emergency situations), 2) partially controlled asthma, 3) patients suffering mental illness or poor compliance, 4) patients with autoimmune disease in remission or with immunodeficiencies, 5) patients with a history of systemic adverse reactions to AIT, and 6) children aged 2–5 years (**Table 1**). In addition, it is possible to continue well-tolerated ongoing AIT during pregnancy, but it is contraindicated to initiate AIT during pregnancy. Furthermore, SLIT is not


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**Table 1.** Indications and contraindications of sublingual immunotherapy

| Indications and contraindications of sublingual immunotherapy |
|---|
| Indications |
| ✓ Patients who have evidence of allergen specific IgE based on allergen skin test or blood allergen specific IgE test and allergic symptoms (allergic rhinitis, asthma, allergic conjunctivitis, etc) induced by allergen exposure. |
| ✓ And satisfies one or more of the criteria below |
| (1) Limited effects on symptom relief by allergen avoidance or pharmacological therapy |
| (2) Intolerable to pharmacological therapy due to the adverse reactions |
| (3) Patients wish to avoid long-term drug use |
| (4) Patients with allergic rhinitis to prevent the onset of asthma and reduce sensitization to new allergens |
| (5) Patients wish to avoid invasive methods such as subcutaneous immunotherapy |
| Contraindications |
| 1. Absolute contraindications |
| ✓ Uncontrolled or severe asthma patients |
| ✓ Patients diagnosed malignancies, refractory active autoimmune diseases |
| ✓ Allergen immunotherapy cannot be initiated in pregnant women* |
| ✓ Eosinophilic esophagitis |
| 2. Relative contraindications |
| ✓ Partly controlled asthma |
| ✓ Patients taking beta-blockers or angiotensin converting enzyme inhibitors |
| ✓ Severe cardiovascular disease (ex. coronary artery disease, severe arrhythmia, uncontrolled hypertension) |
| ✓ Completely resolved systemic autoimmune disease or localized immune disease |
| ✓ Severe psychological impairment or disease |
| ✓ Primary or secondary immunodeficiency |
| ✓ History of systemic reaction to allergen immunotherapy |
| ✓ Children aged under 5 |
| ✓ Low compliance |

IgE, immunoglobulin E.
*Allergen immunotherapy can be continued if treatment is initiated before pregnancy.

recommended for patients with a history of eosinophilic esophagitis, as some of it may be swallowed during the administration of antigen extract tablets or solutions, and eosinophilic esophagitis may occur or worsen as the antigen extract comes into contact with the esophagus during this process.[16,22] When selecting patients, it is recommended to confirm that there are no contraindications in patients with AR for whom antigens clearly related to symptoms have been identified. Additionally, it is important to fully explain the expected effects, side effects, and the duration of SLIT to the patient to ensure their compliance.[14]

## ADMINISTRATION OF SLIT PRODUCTS

### Summary statement

1. Clinically relevant allergens should be selected for SLIT by comprehensively considering the degree of exposure to the allergens and induced symptoms, and evidence of IgE sensitization determined using the skin prick test and serum sIgE test (high).
2. SLIT with house dust mite (HDM) and pollen is effective for the treatment of AR and asthma in adults and children (high).

*Selection of appropriate allergens*

The allergen selection process for SLIT is similar to that of SCIT. That is, it is desirable to select one type or as few allergens as possible that are clinically meaningful to the patient by comprehensively considering the degree of exposure to the allergens, the degree of induced symptoms, and evidence of IgE sensitization using the skin prick test and serum sIgE test.[1]


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While SCIT allows for treatment to be performed by selecting an antigen extract and mixing one or more as needed, SLIT is a method in which a patient purchases and self-administers commercially available allergens. As a result, there is a relatively limited selection of allergens available, and even fewer options for combining them.

*Formulation and administration of SLIT*

Since SLIT exposes the antigen extract to the oral mucosa, the existing formulations include a solution that can be dripped and a tablet that dissolves well in saliva. Standardization of the titer of antigen extracts is important in increasing the clinical efficacy of the treatment. Compared to solution formulations, tablet formulations reduce errors in dosage and can be easily used by patients, thereby increasing administration compliance and standardizing efficacy.[16] Allergens administered in SLIT can be 50–100 times higher than the dose administered in SCIT. Currently, only tablet-form SLITs using HDM and pollen (ragweed and northern pasture grasses like timothy) antigen extracts have been approved by the Food and Drug Administration.

AIT using multi-allergen extracts in polysensitized patients is controversial and is relatively common in North America, but the use of only a single or a small number of related antigens is preferred in Europe. SLIT using multi-allergen extracts may not be effective due to the limited capacity for absorption of the sublingual mucosa, which is supported by a recent report that AIT using a single antigen in polysensitized patients could produce adequate effects.[20] For example, a report showed that SLIT was effective in improving symptoms when performed using timothy extract alone in a patient who was sensitized to various antigens, including timothy and weeds.[23]

For administration, it should be placed under the tongue for at least 1–3 minutes until complete disintegration and then swallowed. In general, a treatment period of at least 3 years is recommended, with subsequent treatment dependent on the individual patient's response.[14] Additional research is warranted to determine the appropriate treatment duration for enhancing outcomes.

*SLIT products available in Korea*

Currently, immunotherapeutic agents for SLIT on the Korean market are products using HDM antigen extracts, which are important antigens in domestic environments (**Table 2**). These include 1) Staroral 300 sublingual solution (Boryeong Biopharma/Stallergenes, allergen extract, HDM), 2) Actair sublingual tablet (Boryeong Biopharma/Stallergenes, allergen extract, HDM), 3) Acarizax 12SQ HDM sublingual tablet (Abbott Korea Co., Ltd., allergen extract, HDM), and 4) Lais tablet (Shinyoung Lofarma/Lofarma, allergoid, HDM).

**Table 2.** SLIT drugs on the market in Korea

| Product name | Staloral | Actair | Acarizax | Lais |
|---|---|---|---|---|
| Allergens | Purified HDM Allergern extract<br>Dermatophagoides farinae 50%<br>Dermatophagoides pteronyssinus 50% | Purified HDM Allergern extract<br>Dermatophagoides farinae 50%<br>Dermatophagoides pteronyssinus 50% | Purified HDM Allergern extract<br>Dermatophagoides farina 50%<br>Dermatophagoides pteronyssinus 50% | Allergoid HDM<br>Dermatophagoides farinae 50%<br>Dermatophagoides pteronyssinus 50% |
| Composition | 10 IR/10 mL/vial,<br>300 IR/10 mL/vial | 100 IR/100 mg/tablet,<br>300 IR/100 mg/tablet | 12SQ | 300 AU/tablet,<br>1,000 AU/tablet |
| Method | Initiation<br>Maintenance | Initiation<br>Maintenance | Single | Initiation<br>Maintenance |
| Pharmaceutical form | Solution | Tablet | Tablet | Tablet |
| Manufacturer | STALLERGENES (Antony, France) | STALLERGENES (Antony, France) | ALK-Abello (Hørsholm, Denmark) | Lofarma (Milan, Italy) |

SLIT, sublingual immunotherapy; HDM, house dust mite.


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## CLINICAL EFFICACY

### Summary statement

1. SLIT showed significant symptom improvement and significantly reduced drug use in patients suffering AR (high).
2. The treatment effect of SLIT is monitored by improvements in symptoms and a decrease in the use of medication. Visual analogue scale (VAS) and combined symptoms and rescue medication scores (CSMS) can be used to evaluate symptomatic changes (high).
3. Serum sIgE and sIgG4 measurements and allergy skin tests can be considered to determine AIT efficacy during follow-ups (very low).

*Clinical efficacy of SLIT*

According to a Cochrane review, SLIT showed significant improvement in symptoms compared to the placebo in AR and significantly reduced the use of medication.[24]

The standardized mean difference (SMD) in the symptom score for AR was reduced by −0.49 (95% confidence interval [CI], −0.64 to −0.34), and the medication score showed a difference of −0.32 (95% CI, −0.43 to −0.21). Most systematic reviews reported that the efficacy of SLIT compared to the placebo was approximately SMD 0.3–0.5, and the effect increased when the treatment period was longer than 12 months (SMD, 0.7).[25]

When comparing the effects of SLIT versus the placebo for seasonal and perennial allergens, the effect size was slightly larger for perennial allergens. AR symptom scores were −0.34 (95% CI, −0.44 to −0.25) for seasonal allergens and −0.93 (95% CI, −1.69 to −0.17) for perennial allergens, and medication scores were −0.30 (95% CI, −0.41 to −0.19) and −0.43 (95% CI −0.89 to 0.02), respectively.[26] When the total nasal symptom score was compared between the treatment and placebo in AR, sublingual tablets improved symptoms significantly more than the placebo for HDM, grass, and ragweed.[27]

*SCIT versus SLIT*

Comparisons of efficacy between SLIT and SCIT mostly conducted through meta-analyses that rely on indirect comparisons, and there are few randomized trials; thus, the evidence on which of the two is more effective is lacking.[25] Among the randomized studies directly comparing SCIT and SLIT against HDM, one study reported that SCIT was more effective in improving symptoms at the end of a 3-year treatment, while another study reported no difference in symptoms and medication scores after a one year of treatment.[28,29] In a network meta-analysis study comparing the 2 immunotherapies for grass allergens, there was no difference between SCIT, SLIT sublingual tablet, and SLIT solution in either the symptom or the medication score for grass pollen.[30] A network meta-analysis on HDM reported a larger effect size for symptom improvement with SCIT compared to SLIT.[31]

*Evaluation of clinical efficacy and proposed biomarkers*

The most important index for determining the efficacy of AIT in AR is CSMS.[32] Six symptoms, including 4 nasal symptoms (nose itching, sneezing, runny nose, and stuffy nose) and 2 eye symptoms (itching/congestion, and tearing), are each scored between 0 and 3. The medication score is scored daily, with oral/topical H1-antihistamines as 1 point, intranasal steroids as 2 points, and oral steroids as 3 points. Symptom scores are converted to a score of 0 to 3 by dividing the total score by 6, and then added to the medication score to calculate the total score. In addition, the SF-12 or SF-36 can be used as a tool for measuring quality of


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life, and the degree of symptom improvement can be evaluated using the rhinoconjunctivitis quality of life questionnaire.[33-35] In actual clinical practice, it is also helpful to use VAS.[1]

Evidence for biomarkers that can be used to monitor treatment effects in SLIT is lacking. Depending on the mechanism of AIT, it is known that serum sIgE decreases and serum sIgG4 increases, but there are also reports stating that the difference between them is less than that of SCIT or that there is no change.[16] In a study that analyzed blood biomarkers after performing SLIT for grass pollen for 2 years, serum sIgE went through an initial increase at 1 month after the start of treatment, and decreased significantly during the treatment period, while serum sIgG4 increased approximately 40-fold at 1 year after treatment initiation and remained constant during the subsequent 12-month period.[36] In another SLIT study on grass pollen, it was reported that memory B cells positive for sIgG2 and sIgG4 increased in the blood after 2–3 years of treatment.[37] Another study reported that the sIgE/tIgE ratio at diagnosis was higher in patients who responded well to immunotherapy than in those who did not.[38] In addition to the above, current studies are attempting to discover biomarkers for SLIT using techniques such as multi-omics analysis using blood samples and sequencing.[36]

## ADVERSE EVENTS AND MANAGEMENT

### Summary statement

1. Patients must be observed in a hospital for 30 minutes after the first dose of SLIT, and equipment capable of handling anaphylaxis and medical supervision are required (low).
2. Information should be provided to patients so that they are aware of the possible adverse events and how to manage them (very low).

SLIT is known to be a safe treatment, and the incidence of systemic adverse events is only approximately 1.1%, which is relatively lower than that of SCIT (2.4%).[39,40] However, caution is required when interpreting this, since adverse events such as anaphylaxis have been reported with SLIT too.[41] After the first dose, the patient must be monitored for at least 30 minutes, and supervision by a medical staff capable of dealing with anaphylaxis is required. Since most adverse events occur at home, patients should be provided with sufficient information to be aware of potential dangers and be able to manage them, especially serious adverse events. If a serious adverse event, such as more than one episode of anaphylaxis, occurs, the benefits and risks of treatment should be discussed again and a decision should be made on whether to continue treatment.[14,42] In cases where uncontrolled severe asthma or exacerbation of asthma due to SLIT is repeated, caution is required.[42]

Transient local mucosal reactions (e.g., pruritus, paresthesia, mucosal swelling, throat irritation) or abdominal pain usually occur at the beginning of treatment.[41] Most localized symptoms are mild and usually resolve spontaneously, with treatment discontinuation in less than 4% to 8% of cases, according to reports.[12,43-45] Treatment may be temporarily discontinued when a patient has undergone a tooth extraction or intraoral surgery, has ulcers or wounds in the mouth, or when an asthmatic patient suffers from an upper respiratory infection, to minimize the chance for adverse events occurring (**Table 3**).


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**Table 3.** Recommendations for possible situations during SLIT

| No. | Possible situations | Expert recommendation |
|---|---|---|
| 1 | Discontinue SLIT for 1–7 days | No need to reduce SLIT dose |
| 2 | Discontinue SLIT for 8–14 days | No need to reduce SLIT dose, but if it is being increased, restart from the first dose. |
| 3 | Discontinue SLIT for > 14 days | Consult with your doctor to determine the next dose, visit the clinic, and take it under the supervision of a medical staff |
| 4 | Scaling | Take SLIT after 24 hrs |
| 5 | Tooth extraction, gum surgery, herpes, stomatitis, oral ulcers, etc. | Stop taking SLIT until completely cured |
| 6 | Enteritis | Stop taking SLIT until completely cured |
| 7 | Moderate to severe hypersensitivity reactions to food or drugs | Stop taking SLIT and consult a doctor within 72 hrs |
| 8 | Beta-blocker | Relative contraindication |
| 9 | MAO inhibitor | Relative contraindication |
| 10 | ACEI | Can be taken |
| 11 | NSAID | Can be taken |

SLIT, sublingual immunotherapy; MAO, monoamine oxidase; ACEI, angiotensin converting enzyme inhibitor; NSAID, nonsteroidal anti-inflammatory drug.

## OPTIMAL TREATMENT DURATION, PREVENTIVE EFFECTS, AND LONG-TERM EFFICACY OF SLIT

### Summary statement

1. The treatment period of SLIT is at least 3 years, and long-term effects persist even after treatment is discontinued (high).

*Optimal duration of therapy*

In most clinical trials evaluating the efficacy of AIT, patients were followed up for 1–2 years after treatment. In a study of SLIT for grass pollen, a 3-year treatment followed by a 2-year follow-up period showed sustained benefits.[46-49] In a SLIT study on HDM, the positive effects persisted even 1 year after the treatment,[50] and a study comparing the results from 1-, 2-, and 3-year treatments showed the greatest clinical benefit for the 3-year treatment.[51] At least 3 years of treatment is recommended to obtain long-term effects following the discontinuation of treatment.

The treatment period of AIT should be determined individually, considering the patient's clinical response, severity, history of adverse events, and preferences.[52] Their response to AIT should be periodically assessed, and considering recurrence after the discontinuation of AIT, the therapeutic benefits, and the associated convenience, treatment lasting for more than 3 years is recommended.

*Preventive effects*

The preventive effect of SLIT on asthma was mainly studied in pediatric patients with AR, and SLIT effectively reduced the incidence of asthma and sensitization to new antigens.[53,54] Compared to those who received a 3-year SLIT therapy, the control group that did not receive AIT had a 3.8-fold higher incidence of asthma after 3 years.[54] In pediatric patients with airway hyperresponsiveness, the rate of positive methacholine provocation tests decreased after SLIT.[53] However, a randomized clinical trial published in 2018 demonstrated that SLIT showed no significant difference in time to onset of asthma in the 812 pediatric patients diagnosed with grass pollen AR.[49]


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When SLIT was performed for 3, 4, and 5 years in patients sensitized to HDM antigen alone, and the control group was sensitized to at least one new antigen, the treatment group showed lower values of new sensitization than those of the control group, with 21.4%, 12.5%, and 11.7%, respectively, and the frequency of new sensitization decreased as the treatment period increased.[55] When SLIT against HDM (Der p 1 and Der p 2) and pollen (Phl p 1, Par j 1, and Bet v 1) was compared with the control group that received drug treatment alone, the new antigen sensitization was found to be significantly lower in the SLIT group (3.1% vs. 34.8%; odds ratio [OR], 16.85; 95% CI, 5.73, 49.13), and mild persistent asthma also occurred less frequently (1.5% vs. 28.8%; OR, 0.04; 95% CI, 0.01, 0.17).[53]

*Long-term efficacy*

Whether the therapeutic effect persists after the discontinuation of SLIT has been demonstrated in many randomized clinical trials.[56] When SLIT for grass pollen was administered for 3 years and followed up, symptoms improved and drug use decreased even 4 years after the end of treatment.[57] In the case of 3 years of SLIT against HDM, the clinical effect persisted for 7 years after treatment, and in the case of patients who received 4 or 5 years of treatment, the clinical effect lasted for 8 years.[55]

## SUMMARY AND CONCLUSION

AIT is a treatment that reduces or eliminates allergic symptoms in patients by inducing resistance to allergens by gradually increasing the dose of the causative allergen. It is the only fundamental treatment method to date that can induce a cure or improve the course of allergic diseases. SLIT has the advantage of reducing the risk of systemic adverse events caused by the injection of traditional SCIT and allowing self-administration at home. Recently, the dosage form has changed from a solution to a tablet formulation, and clinical studies published to date have shown that this is an effective and safe treatment for AR and asthma. Through this guideline, the authors expect that clinicians who intend to, or are already, performing SLIT, can actively treat allergic diseases by gaining a deeper understanding of the mechanism of SLIT, and selection of treatment targets according to the patient's condition or preference, treatment effects, adverse events and managements, and long-term efficacy.

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