



YONSEI
UNIVERSITY

알레르기 면역치료의 실전적 방법

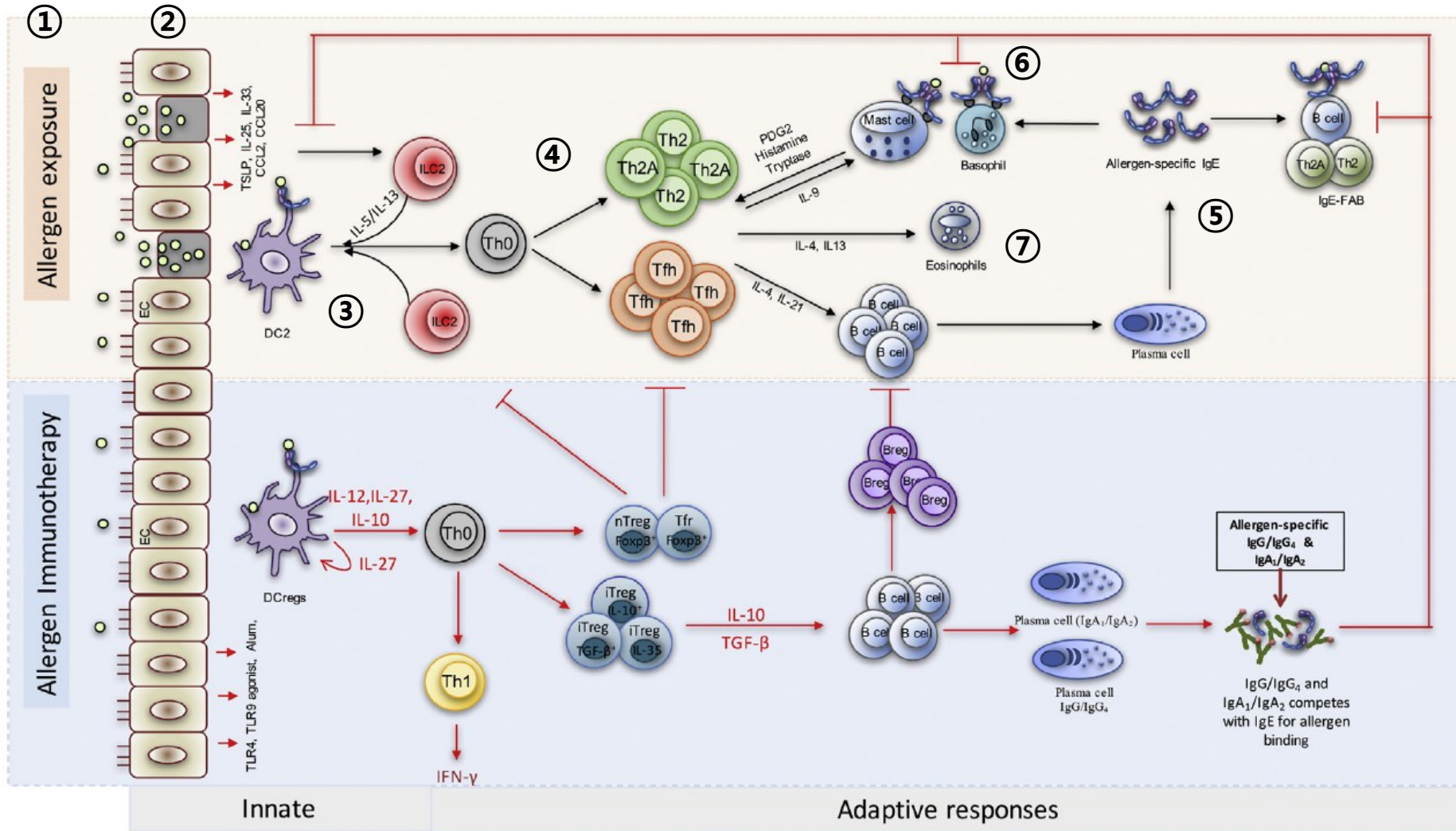
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Allergy and Asthma Center, Severance Hospital,
Yonsei University College of Medicine

Severance

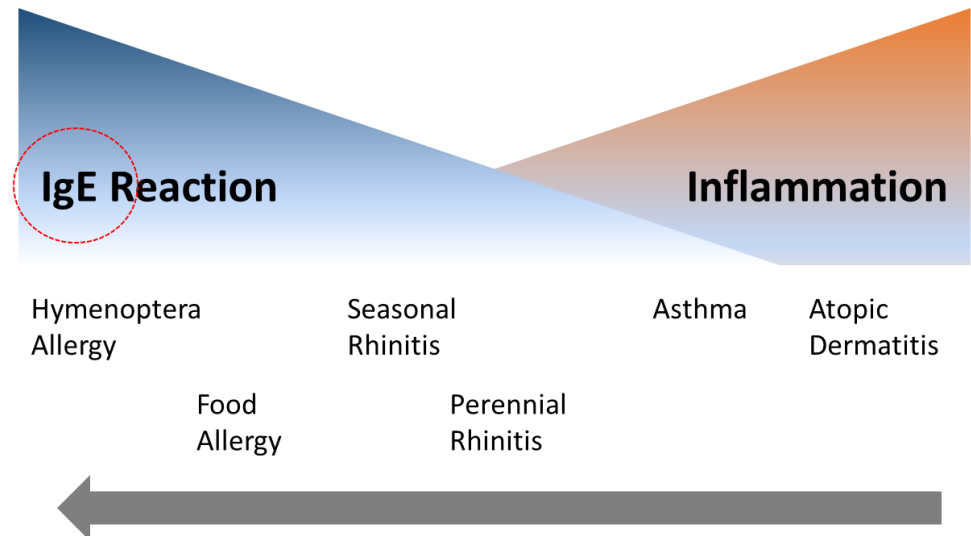
Mechanisms of AIT

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Disease Indications for AIT

- Allergic rhinitis
- Allergic conjunctivitis
- Allergic asthma (mild, well controlled)
- Atopic dermatitis (aeroallergen)
- IgE-mediated food allergy (일부)
- Hymenoptera venom allergy



Allergen indications for AIT

- Well standardized Allergens
- Seasonal
 - 봄: Trees (birch, oak, alder..)
 - 여름: Grasses (timothy, rye, bermuda..)
 - 가을: Weeds (Hop J, mugwort, ragweed..)
- Indoor Perennial: HDM, Cat, Dog, Cockroach 등
- Hymenoptera venom
- Fungus (*Alternaria*)

Allergen indications for AIT

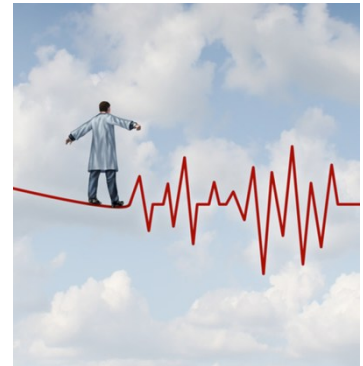
- Allergens not capable of immunotherapy
 - 환삼덩굴 (*Humulus japonicus*): 가을
 - 일본 삼나무 (Japanese cedar) : 봄 (일본에서는 SLIT 사용 중)
 - Bee venom: 희귀의약품센터
 - 항원의 수급 상황에 따라 변동이 있을 수 있음



CEDARCURE[®] Japanese Cedar Pollen Sublingual Tablets launched by Torii in June 2018 is the sublingual immunotherapy drug for Japanese Cedar Pollinosis and regulatory approved sublingual tablet available for adult and pediatric patients.

Contraindication of AIT

- Uncontrolled or severe asthma (+/- COPD)
- Active, systemic autoimmune disorders (unresponsive to treatment)
- Active malignant dz.
- AIT initiation during pregnancy
- Recent MI, HF, malignant HTN 등으로 에피네프린 사용 불가능한 환자



Relative Clx. (환자 별로 AIT 의 risk/benefit 을 고려해서 결정)

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- Partially controlled asthma
- Beta-blocker therapy (local or systemic)
- Severe cardiovascular diseases (eg. CAOD)
- Systemic autoimmune disorders in remission or organ specific
- Severe psychiatric disorders
- Poor adherence
- Primary and secondary Immunodeficiency
- History of serious systemic reactions to AIT

Table 2 Absolute (A) and relative (R) contraindications for AIT

Medical condition	Aeroallergens		Venom immunotherapy
	SCIT	SLIT	
Asthma (partially controlled)	R	R	R
Asthma (uncontrolled)	A	A	A
Autoimmune disorders in remission	R	R	R
Autoimmune disorders in active forms (nonresponding to treatment)	A	A	A
Malignant neoplasias	A	A	R
β-Blockers	R	R	No
ACE inhibitors	No	No	R
MAOIs	No	No	No
Cardiovascular diseases	R	R	No
Pregnancy (initiation of AIT)	A	A	A
Pregnancy (continuation of AIT)	No	No	No
Children (<2 years of age)	A	A	A
Children (2–5 years of age)	R	R	R
Any other age groups	No	No	No
HIV (A, B stages; CD4+ >200/μl)	R	R	R
AIDS	A	A	A
Psychiatric and/or mental disorders	R	R	R
Chronic infections	R	R	R
Immunodeficiencies	R	R	R
Use of immunosuppressive drugs	R	R	R

Routes of AIT



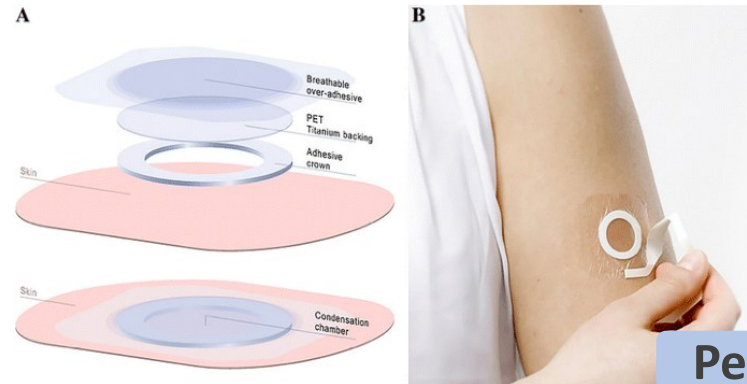
Subcutaneous Immunotherapy (SCIT)



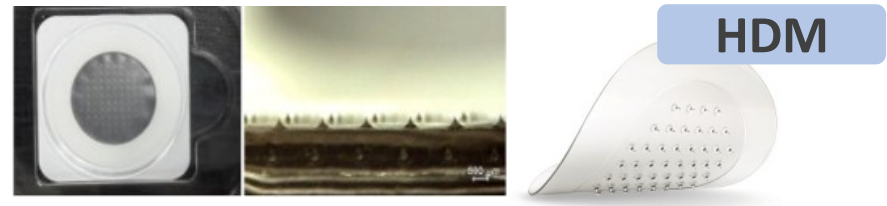
Sublingual Immunotherapy (SLIT)



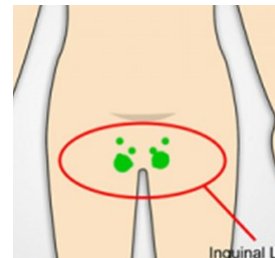
Oral IT (OIT)



Epicutaneous Immunotherapy (EPIT)

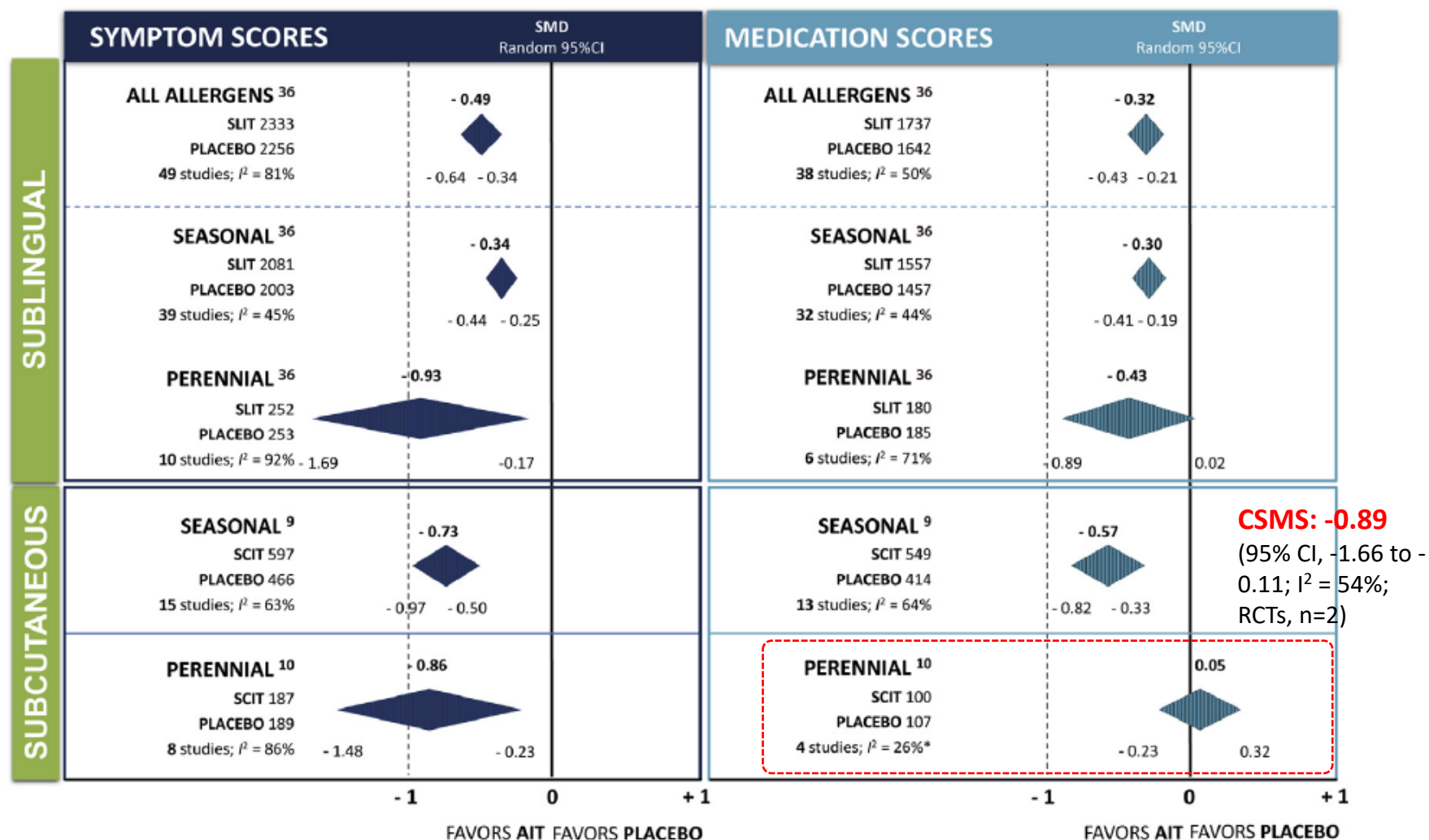


Transdermal Immunotherapy (TDIT)



Intralymphatic IT (ILIT)

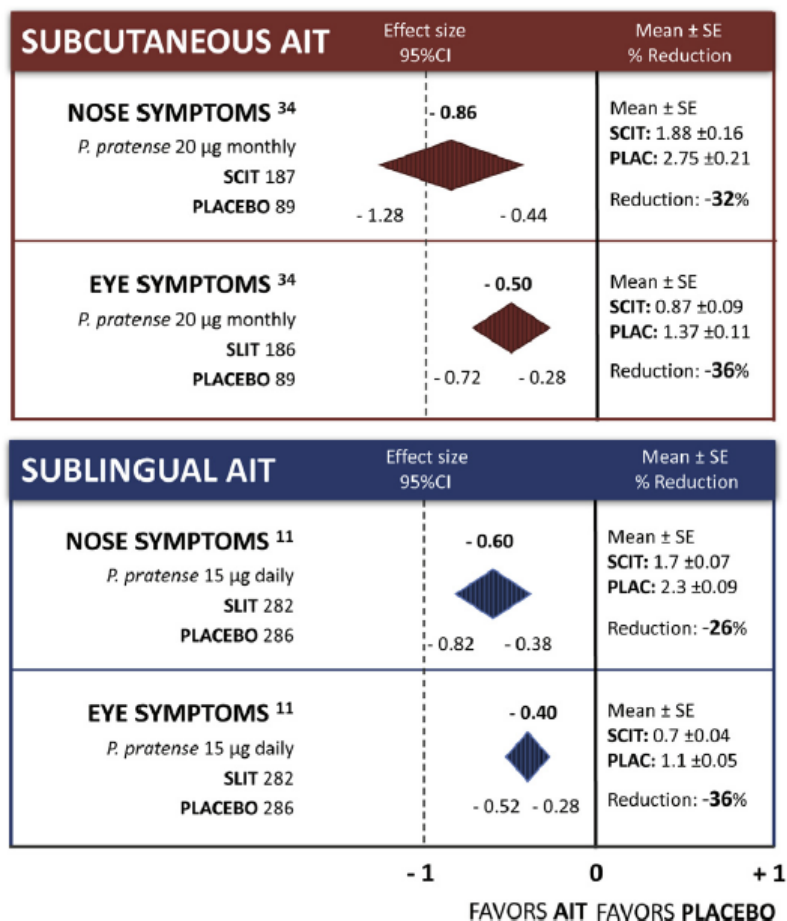
SCIT or SLIT?



SCIT or SLIT? : 2 well-powered RCT 비교

대상: moderate-to-severe grass pollen SAR for at least 2 years

항원: same standardized single-allergen *Phleum pratense* extract



20 μ g of the major allergen Phl p 5
Cluster IT

S/E: mild grade 2 17.2%
non-life-threatening
grade 3 reactions in 4.4%

15 μ g of the major allergen Phl p 5

S/E: oral pruritis in 46%
mouth edema in 18%
→ 4% 는 SLIT 중단

SCIT or SLIT? : Head-to-head double-blind, controlled trials of SLIT versus SCIT for AR

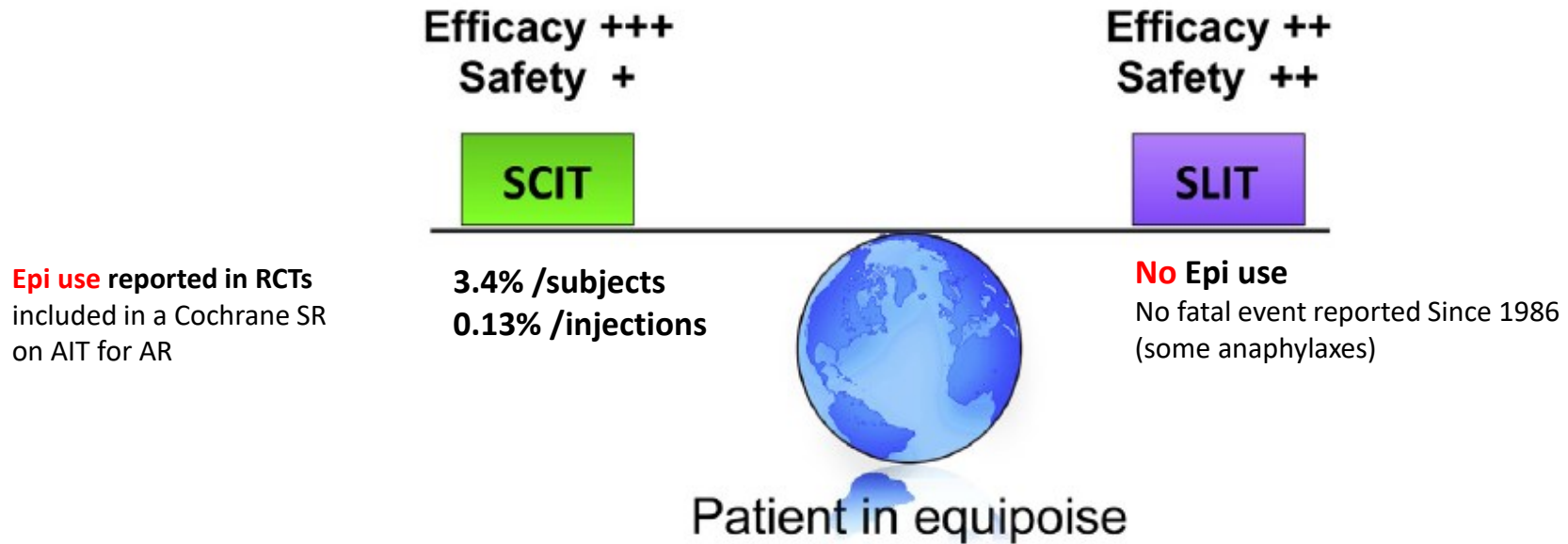
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First author, year, country	Study design	Allergen	No. of groups	SLIT group (no.)	SCIT group (no.)	Placebo group (no.)	Age (y)	Inclusion criteria	Asthma	Sensitization status
Klinchi et al, ⁴⁷ 2004, Denmark	Randomized, double-blind, double-dummy, placebo controlled study	Birch (Bet v 1)	3	23	24	24	30 (20-58)	1. 2 y of birch-associated ARC 2. Positive sIgE level, conjunctival provocation test result, and SPT response to birch pollen	SLIT: 39% SCIT: 29% Placebo: 37%	1. HDM sensitization: 11% to 14% 2. Grass pollen symptoms June-July: 38% to 56%
Quirino et al, ⁴⁸ 1996, Italy	Double-blind, double-dummy controlled study	Grass mix	2	10	10	—	27 (13-39)	1. Clinical history of grass pollen sensitization 2. Positive sIgE level and SPT response to grass pollen	SLIT: 80% SCIT: 80%	1. Patients sensitized to other inhalant allergens were excluded.
Ventura et al, ⁴⁹ 2009, Italy	Randomized, double-blind, placebo-controlled study	<i>Juniperus ashei</i>	4	10	10	SL: 10 SC: 10	39 ± 2.4 (18-55)	1. ARC correlated with the cypress pollen season. 2. Positive sIgE level and SPT response to grass pollen	SLIT: NA SCIT: NA	1. Participants in this study were monosensitized to cypress.
Yukselen et al, ³⁸ 2012, Turkey	Randomized, double-blind, double-dummy, placebo-controlled study	<i>D pteronyssinus</i> and <i>D farinae</i>	3	11	10	10	SLIT: 9.2 ± 3.4 SCIT: 10.9 ± 3.2 Placebo: 10.1 ± 2.7	1. Clinical history of at least 1 year of rhinitis with asthma associated with HDM. 2. Positive sIgE level and SPT response for both <i>D pteronyssinus</i> and <i>D</i>	SLIT: 100% SCIT: 100%	1. Participants included in this trial were monosensitized to HDM.

First author, year, country	SLIT									SCIT								
	Build-up phase			Maintenance phase				Units	SLIT method	Build-up phase			Maintenance phase				Units	Placebo
	Frequency	Dose	Duration	Frequency	Dose	Duration	Cumulative dose			Frequency	Dose	Duration	Frequency	Dose	Duration	Cumulative dose		
Klinchi et al, ⁴⁷ 2004, Denmark	Every second day	Initial: 0.0164 µg Top: 49.2 µg of Bet v 1	30 days	Every second day	49.2 µg of Bet v 1	21-23 months	11.18 mg of Bet v 1	µg	SLIT: Swallow Drops	Weekly	Initial: 0.0164 µg Top: 3.28 µg of Bet v 1	12 weeks	Monthly	3.28 µg of Bet v 1	21 months	51 µg of Bet v 1	µg	Caramelized sugar (drops) and histamine dihydrochloride (injection)

No significant differences were observed between SLIT and SCIT groups (birch, 2y)

SCIT or SLIT?



	SCIT	SLIT
아나필락시스 위험성	있음	거의 없음
약물 투여	병원	가정
알레르겐 혼합	매우 쉬움	제한적
사용 가능한 알레르겐	다수	제한적
효과	증명됨	증명됨
질병 조절 효과	있음	있음

SCIT, 어떤 제품을 선택할 것인가

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SCIT, 어떤 제품을 선택할 것인가

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미국



유럽





Allergen extracts as compounding sterile preparations (CSPs) are single-dose and multiple-dose *intradermal or subcutaneous injections* that are prepared by specially trained physicians and personnel under their direct supervision. Allergen extracts as CSPs are not subject to the personnel, environmental, and storage requirements for all CSP microbial contamination risk levels in this chapter only when all of the following criteria are met:

1. Before beginning compounding activities, personnel perform a thorough hand-cleansing procedure by removing debris from under fingernails (using a nail cleaner under running warm water), followed by vigorous hand and arm washing to the elbows for at least 30 seconds with either nonantimicrobial or antimicrobial soap and water.
2. Compounding personnel wear hair covers, facial hair covers, gowns, and face masks.
3. Compounding personnel perform antiseptic hand cleansing with an alcohol-based surgical hand scrub with persistent activity.
4. Compounding personnel wear powder-free sterile gloves that are compatible with sterile 70% isopropyl alcohol (IPA) before beginning compounding manipulations.
5. Compounding personnel disinfect their gloves intermittently with sterile 70% IPA when preparing multiple allergenic extract as CSPs.
6. Ampule necks and vial stoppers on packages of manufactured sterile ingredients are disinfected by careful wiping with sterile 70% IPA swabs to ensure that the critical sites are wet for at least 10 seconds and allowed to dry before they are used to compound allergen extract as CSPs.
7. The label of each multidose vial of allergen extract as CSPs lists the name of 1 specific patient, a beyond-use date, and storage temperature range that is assigned based on manufacturer's recommendations or peer review publications.
8. Single-dose allergen extract as CSPs shall not be stored for subsequent additional use.

Serial dilution to 1:10,000

Allergen extract

Diluent

1:1 1:10 1:100 1:1,000 1:10,000

0.5 ml 5.0 ml

SCIT, 어떤 제품을 선택할 것인가

	Hollister-Stier [□]	Novo-helisen/ Allergovit [□]	Tyrosine S [□]
제조사	Hollister-Stier (USA)	Allergopharma (독일)	Allergy Therapeutics (UK)
국내 판매사	원메디칼	알레파인터내셔널	신광신약
항원 선택	의사	의사	의사
항원 Mix	의료진	회사 (완제품)	회사 (완제품)
Formulation	Non-modified	Non-modified (HDM) Allergoid preparation (Pollen)	Non-modified
Adjuvant	None	Aluminum hydroxide adsorbed	L-Tyrosine
Standard unit	Allergy units (AU)	Therapeutic units (TU)	TU

Table 1. Comparison of the Differences Between US and European Allergen Extracts and Specific Immunotherapy Practice Patterns

Variable	United States	Europe
Regulatory agency	FDA	EMA
Standardization		
Method	ID ₅₀ EAL	Nordic
Test technique	Intradermal	Percutaneous
End point	Extract dilution that produces sum of erythema of 50 mm	Extract dilution that produces a wheal equal to the histamine control
Potency determination	Comparison with CBER reference control	Compared with in-house reference
Future focus	Overall allergenicity	Major allergen content
Potency units	BAU, wt/vol, PNU, milligrams of major allergen for ragweed and cat	Varies; each company essentially has its own potency units, some provide milligrams of major allergen
Extract formulation		
Location	Prepared in physicians offices	Prepared at extract manufacturer site
No. of allergens	Multiple	Generally 1
Allergen extract types	Aqueous and glycerinated unmodified extracts, alum-precipitated depot extracts	Approximately 100% depot extract, 20% allergoid, <5% adjuvants
SLIT	Approximately 5.9% of allergists, no FDA approved formulation	Approximately 45% of prescribed SIT, solution and tablets available, some are registered
Reimbursement	Covered as a medical service by government and private insurers, prices can be negotiated but private insurers often use government schedule	Varies, extract companies negotiate coverage with each country

Abbreviations: BAU, bioequivalent allergy units; CBER, Center for Biologics Evaluation and Research; EMA, European Medicinal Agency; FDA, Food and Drug Administration; PNU, protein nitrogen units; SIT, specific immunotherapy; SLIT, sublingual immunotherapy.

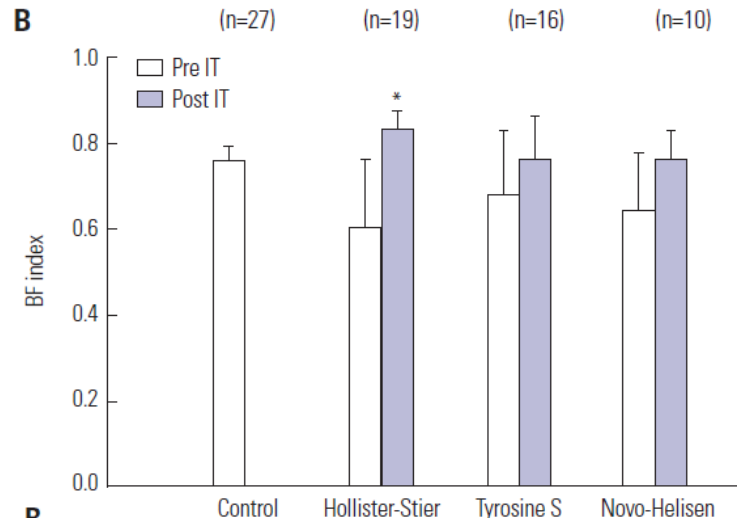
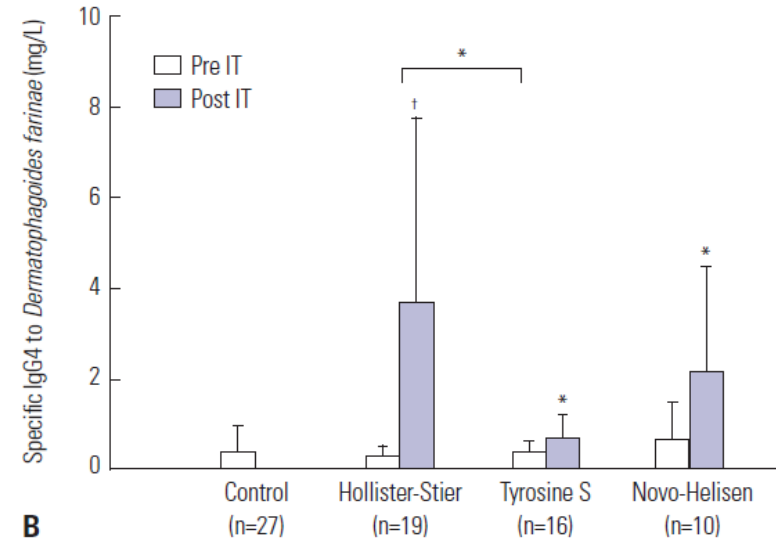
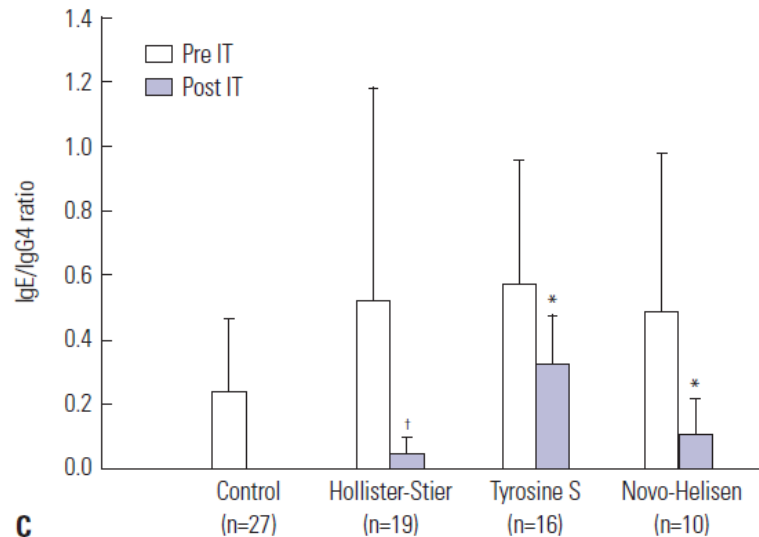
Table 1. Extract Potency Definitions as Stipulated by CBER of the FDA and Most European Allergen Extract Manufacturers

Manufacturer	Products	Potency expression	Units Based on	Parameters
CBER	Allergens	(B)AU	Intradermal test in highly allergic patients. No control.	Erythema size, 50 mm total of 2 diameters, arithmetical mean.
ALK	Allergens for SLIT and depot for SCIT	BU, HEP, STU, and SQ-U	BU: SPT in 30 allergic patients. No control. HEP: same with histamine control of 10 mg/mL. STU and SQ-U: based on therapeutic response.	100 BU = produces a wheal with a mean average size of 70 mm ² . HEP = concentration that gives same reaction as histamine control.
Allerbio	Allergens	IR	SPT with 3 serial 1/10 dilutions in allergic patients. 9% codeine phosphate is control (6 mm).	100 IR = concentration that gives geometrical mean diameter of wheal same as control (6 mm).
Allergopharma	Allergens, SCIT: Allergoids and depot	SBU	SPT in allergic patients 0.1% histamine control.	1,000 BU = concentration that gives the same wheal as control.
Allergy Therapeutics	Allergens, allergoids	DU/TU and SU for allergoids	SPT in 25 allergic, 15 atopic and 10 healthy people.	10,000 DU is value with lowest false-positive and false-negative results. Fixed DU/TU relation for each allergen.
HAL Allergy	Allergens, SCIT: Allergoids and depot	(B)AU	Intradermal test in 15 highly allergic patients, chosen from a pool of patients. No control.	Erythema size total of 2 diameters, arithmetical mean of 50 mm = D ₅₀ .
IPI-ASAC	Allergens, SCIT: Polymerized and depot	UBE	Duplicate SPT with 3 serial 1/10 dilutions in 20-30 allergic patients, negative and histamine, 0.10-mg/mL, control.	Mean concentration provoking a wheal equivalent to histamine control \times 10,000 = UBE.
Leti	Allergens, SCIT: Allergoids and depot	HEP _L	Duplicate SPT in at least 20 allergic patients, 10-mg/mL histamine control.	10 HEP _L = concentration that gives a wheal equivalent to 10 mg/mL of histamine.
Stallergènes	Allergens, SCIT: depot	IR	Quadruple SPT with 3 serial 1/10 dilutions in 30 allergic patients. Control is 9% codeine phosphate (7 mm).	100 IR = concentration with a geometrical mean diameter of wheal size same as control (7 mm).

Table 2. Baseline Characteristics of the Patients

	Total (n=72)	Hollister-Stier® (n=19)	Tyrosine S® (n=16)	Novo-Helisen® (n=10)	Control (n=27)	p value
Age (yr)	30.1±10.8	31.1±11.3	26.5±10.6	29.4±12.2	31.8±10.0	0.397
Sex (M:F)	33:39	8:11	8:8	4:6	13:14	0.936
Asthma, n (%)	26 (36.1)	9 (47.4)	4 (25.0)	4 (40.0)	9 (33.3)	0.552
Allergic rhinitis, n (%)	53 (73.6)	19 (100.0)	3 (18.8)	8 (80.0)	23 (85.2)	<0.001
Atopic dermatitis, n (%)	23 (31.9)	2 (10.5)	13 (81.3)	3 (30.0)	5 (18.5)	<0.001
Pre IT sIgE to D.f (kU/L)	44.6±37.6	36.7±27.8	75.1±36.5	58.9±36.7	26.8±32.5	0.001
Pre IT sIgG4 to D.f (mg/L)	0.4±0.5	0.3±0.2	0.4±0.2	0.6±0.8	0.4±0.6	0.112
Post IT sIgE to D.f (kU/L)	61.8±38.0	50.1±39.8	77.3±33.4	56.7±36.6	NA	0.194
Post IT sIgG4 to D.f (mg/L)	2.3±3.1	3.7±4.1	0.7±0.5	2.2±2.3	NA	<0.001
IT duration (months)	13.9±6.6	15.2±6.7	12.8±3.6	13.4±9.7	NA	0.362
IT maintenance dose, mean (range)		761.8 AU (432–1600 AU)	14999.4 TU (6666.4–16666 TU)	3057.1 TU (1600–5000 TU)	NA	NA

AU, Allergy unit; D.f, *Dermatophagoides farinae*; IT, immunotherapy; NA, not available; TU, Therapeutic unit; sIgE, specific immunoglobulin E. p value was calculated by Kruskal-Wallis test, Fisher's exact test.



Prescription for SCIT

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좌측의 농도는 권장농도입니다		
	처방 농도(ml)	비고
D.p & D.f mixture (각 15,000 AU/ml)	0.40 mL	0.4
Ap Dog (180 mcg/ml)	0.50 mL	0.5
Ap Cat (10,000 BAU/ml)	2.00 mL	2
Cockroach (1:10 w/v)	0.50 mL	
Sagebrush/Mugwort (1:20 w/v)	0.50 mL	0.5
Ragweed Mixture (1:20 w/v)	0.50 mL	
Boxelder/Maple Mix (1:20 w/v)	0.50 mL	
Birch Mix (1:20 w/v)	0.50 mL	0.5
Oak Mix (1:20 w/v)	0.50 mL	
Timothy grass (100,000 BAU/ml)	0.35 mL	
Bermuda grass (10,000 BAU/ml)	0.50 mL	
Rye grass (10,000 BAU/ml)	0.50 mL	
Alternaria (1:10 w/v)	0.50 mL	
Diluent		1.1

Total 5.0 mL
희박하는 희석 시작 배율 ○ 원액 ○ 1 : 1,000 ● 1 : 10,000

기록자명 박경희

SPECIFIC IMMUNOTHERAPY ORDER FORM

환자명 (한글): 김** (영) KIM ***** ID : 56***** sex/Age F/20		병원명 : 세브란스 병원 DEPT 알레르기내과 (TEL.) : 02-2228-5*** 처방날짜 2018.08.07	
<input checked="" type="checkbox"/> INITIAL TREATMENT	<input type="checkbox"/> MAINTENANCE TREATMENT	* DOCTOR'S SIGNATURE	

1) SEASONAL VACCINE			* N.B. NO MORE THAN 4 ALLERGENS PER VACCINE		
No.	MIXTURES	Composition Treat	No.		
006	Grasses		123	Wall pellitory	
015	Grasses / Cereals		126	Oat	
			129	Hazel	
			133	Velvet grass	
			135	Bermuda grass	
			140	Orchard grass	
			142	Linden	
			143	Dandelion	
			151	Olive	
			152	Poplar	
			153	Plane tree	
			154	Ragweed	
			157	Rye grass	
			158	Rye	
			168	Elm	
			169	Engl. Plantain	
			170	Willow tree	
			173	Wheat	
			177	Timothy grass	
			178	Kentucky blue	
			179	Meadow fescue	
			190	Saltwort	

2) PERENNIAL VACCINE			* N.B. NO MORE THAN 4 ALLERGENS PER VACCINE		
No.	EPITHELIA/FEATHER	Composition Treat	No.	MOULDS	Composition Treat
306	Dog	20	400	Alternaria	
309	Cat	20	401	Aspergillus	
314	Horse		402	Botrytis	
317	Cow		405	Cladosporium	
			406	Curvularia	
			407	Fusarium	
			408	Helminthospor.	
			410	Mucor	
			412	Penicillium	
			413	Pullularia	
			414	Rhizopus	
			416	Serpula	

* Seasonal and perennial allergens should not be mixed.



TYROSINE S ORDER FORM

Ref No. _____

PATIENT NAME _____ DATE(처방일) _____

DATE OF BIRTH _____ (If no date is given FULL strength vaccine will be supplied)

Please tick box if patient's symptoms are very severe (a dilute vaccine will be supplied)
Seasonal Asthma ☐ Perennial Asthma ☐ Hayfever ☐
Perennial Rhinitis ☐ Other Compliant _____
Very Severe ☐ Moderately Severe ☐ Mild ☐

CONTROL REACTIONS Prick _____ Intra Dermal _____
Treatment to Commence _____ Physician's Signature _____

Tyrosine S Treatment Course ☐ <- Please tick box for chosen course.
Tyrosine S Continuation Course ☐

POLLENS		MOULDS	
1. 4006 Nettle 쑥기풀		17. 1100 Alternaria alternata 알타리나리아	
2. 4007 Plantain 질경이		18. 1300 Cl. Cladosporioides 클라도스포리움균	
3. 4100 B2 Grass 잔디화분류			
4. 4201 Alder 오리나무		INSECTS	
5. 4202 Ash 물푸레나무		19. 2705 Cockroach 바퀴벌레	
6. 4203 Beech 너도밤나무			
7. 4204 Birch 자작나무		HOUSE DUST MITES	
8. 4207 Hazel 개암나무		20. 2800 D.farinae 복미집먼지진드기	
9. 4209 Oak 참나무		21. 2801 D.pteronyssinus 유합집먼지진드기	
10. 4210 Plane 버즘나무			
11. 4503 Fat hen 명아주		HAIRS & FURS	
12. 4801 Mugwort 쑥		22. 3203 Horse hair 말털	
13. 4957 Ragweed 돼지풀		23. 3204 Cat fur 고양이털	
14. 4961 Cult.Rye 경작호밀		24. 3205 Dog hair 개털	
15. 4982 Olive pollen 올리브나무			
16. 4983 Parietaria pollen 개들톱이		CONTROLS	
		6370 Histamine 히스타민	
		1908 Control 프릭컨트롤	

Hospital or Clinic Name _____
Address _____

Please ensure that all entered on this form in order to prevent unnecessary correspondence and delay

SCIT 백신 – 조제시 주의점

- H 사 제품에 한함
- 이외 제품은 처방전만 작성
- 혼합 가능 알레르겐
 - 집먼지진드기
 - 꽃가루
 - 동물털
- 혼합 불가능 알레르겐
 - 바퀴
 - 곰팡이
- 보관
 - 4°C 냉장보관



- Conventional IT

- 1회 / 1일, 1주 간격, 초기치료 기간 3-4개월



- Cluster IT

- 2-4회 / 1일, 1주 간격, 초기치료 기간 1-2개월



- Rush IT

- 1회 / 1-2 시간 간격, 초기치료 기간 3-4일 (입원)



- Ultra-rush IT

- 1회 / 30분-1시간 간격, 초기치료 기간 1일 (입원)





30분 관찰

Adverse reaction monitoring (SCIT)

TABLE I. World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System (see text)

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
<p><i>Symptom(s)/sign(s) of 1 organ system present*</i></p> <p><u>Cutaneous</u> Generalized pruritus, urticaria, flushing, or sensation of heat or warmth† or Angioedema (not laryngeal, tongue or uvular) or <u>Upper respiratory</u> Rhinitis - (eg, sneezing, rhinorrhea, nasal pruritus and/or nasal congestion) or Throat-clearing (itchy throat) or Cough perceived to originate in the upper airway, not the lung, larynx, or trachea or <u>Conjunctival</u> Erythema, pruritus or tearing <u>Other</u> Nausea, metallic taste, or headache</p>	<p><i>Symptom(s)/sign(s) of more than 1 organ system present</i></p> <p>or <u>Lower respiratory</u> Asthma: cough, wheezing, shortness of breath (eg, less than 40% PEF or FEV₁ drop, responding to an inhaled bronchodilator) or <u>Gastrointestinal</u> Abdominal cramps, vomiting, or diarrhea or <u>Other</u> Uterine cramps</p>	<p><u>Lower respiratory</u> Asthma (eg, 40% PEF or FEV₁ drop NOT responding to an inhaled bronchodilator) or <u>Upper respiratory</u> Laryngeal, uvula, or tongue edema with or without stridor</p>	<p><u>Lower or upper respiratory</u> Respiratory failure with or without loss of consciousness or <u>Cardiovascular</u> Hypotension with or without loss of consciousness</p>	<p>Death</p>
		<p><Prepped medication> Pheniramine Dexamethasone Epinephrine (0.3 ~ 0.5 mL, IM) Salbutamol (evohaler)</p>		

SLIT, 어떤 제품을 선택할 것인가

SLIT 제품	초기치료	유지치료
엑트에어 (Actair) Tablet, 실온보관	2일: 1T (100IR)→ 2T	매일 1T (300 IR)
스타로랄 (Staloral) Drop, 냉장보관	11일 Blue>1→2→4→6→8→10drops Purple>1→2→4→6→8drops	매일: 보라색 4 방울 or 주3회: 보라색 8방울
라이스 (Lais) Tablet, 실온보관	4일 1T → 2T → 3T → 4T	주1회: 2T or 주2회: 1T-1T
슬릿원 (Slitone) Drop, 실온보관	구분 없음. 매일 하나씩 (0.2ml=약 5방울)	

Comparing SLITs

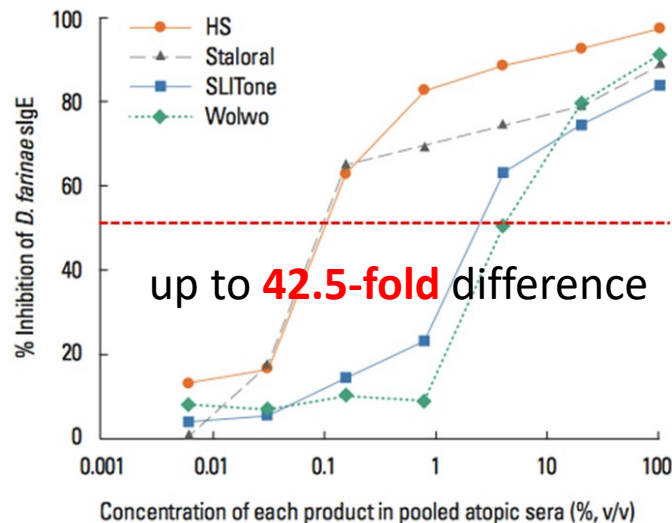
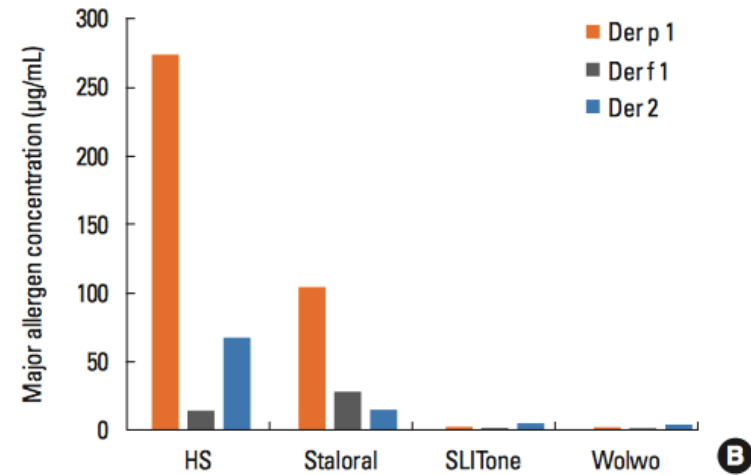
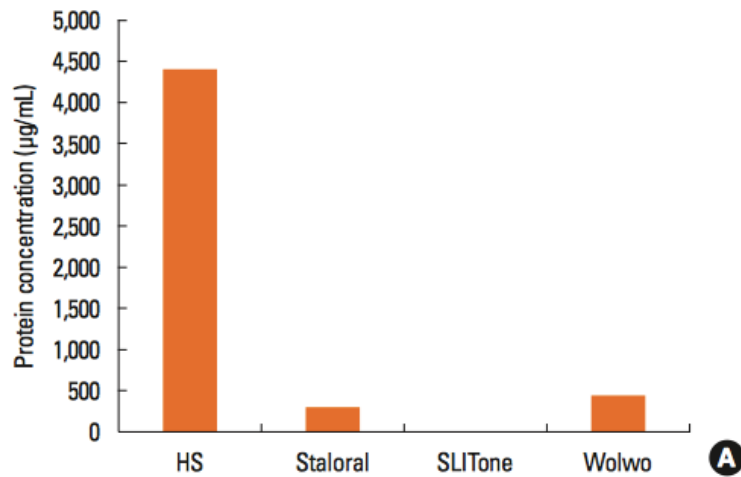


Table 2 Cumulative doses of total protein and major allergens after 28-day treatment using 4 different products

	Total protein (µg)	Der p 1 (µg)	Der f 1 (µg)	Der 2 (µg)
Staloral [®]	3,276.90	1,169.28	309.12	164.64
SLITone [®]	9.58	19.04	3.36	19.60
Wolwopharma [®]	2,507.12	14.00	2.80	16.24
Hollister-Stier [®]	879.70	54.86	2.72	13.28

TABLE II. Grading system for SLIT local AEs (see [Table III](#) for the Medical Dictionary for Regulatory Activities codes)

Symptom/sign (see Table I)	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Unknown severity
Pruritus/swelling of mouth, tongue, or lip; throat irritation, nausea, abdominal pain, vomiting, diarrhea, heartburn, or uvular edema	<ul style="list-style-type: none">• Not troublesome AND <ul style="list-style-type: none">• No symptomatic treatment required AND <ul style="list-style-type: none">• No discontinuation of SLIT because of local side effects	<ul style="list-style-type: none">• Troublesome OR <ul style="list-style-type: none">• Requires symptomatic treatment AND <ul style="list-style-type: none">• No discontinuation of SLIT because of local side effects	<ul style="list-style-type: none">• Grade 2 AND <ul style="list-style-type: none">• SLIT discontinued because of local side effects	The treatment is discontinued but there is no subjective and/or objective description of the severity from the patient/physician

Each local AE can be early (<30 min) or delayed.

- In cases of oral inflammation, such as mouth ulcers, lichen planus, or dental extractions, administration of SLIT be temporarily discontinued until there is “complete healing of the oral cavity.”
- Prescribe epinephrine (only FDA, not usual practice in EU)

Risk factors for systemic reactions during AIT

■ Patient Factors

- Current allergy symptoms & potential allergen exposure
- Current infections
- Uncontrolled or severe asthma
- A high degree of sensitization
- Mast cell disease
- Beta-blockers use
- High-intensity physical exercise
- Previous systemic reaction to SCIT or SLIT

1,201 AAAAI members

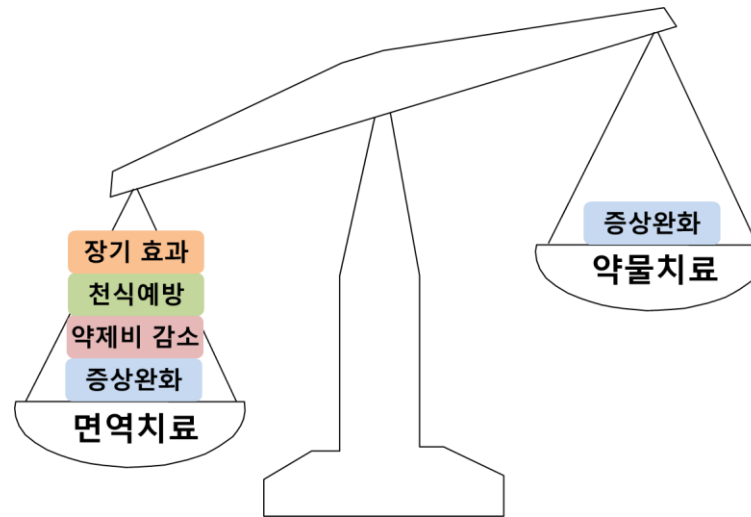
Table 2

Practitioners who dose adjust during pollen season

Characteristics	Proportion who dose adjusted during pollen season	P
Country of practice		
USA (N = 508)	199 (39%)	.001
Europe (N = 16)	13 (81%)	
Canada (N = 21)	13 (62%)	
Other (N = 40)	15 (6%)	
Years in practice		
<10 years (N = 193)	66 (34%)	.02
>10 years (N = 391)	175 (45%)	
Practice area		
Urban (N = 232)	109 (47%)	NS
Suburban (N = 320)	121 (38%)	
Rural (N = 35)	12 (34%)	
Practice setting		
Academic (N = 167)	72 (43%)	NS
Non-academic (N = 416)	167 (40%)	
Number of SCIT patients		
<100 (N = 156)	65 (42%)	NS
100–400 (N = 234)	91 (39%)	
>400 (N = 174)	82 (47%)	

■ Physician Factors

- Poor injection technique
- Overdose of allergen extract
- Excess dose escalation during initiation
- Failure to follow manufacturer's recommendation for dose reduction when change to new production batch



- Disease, Allergen Indications
- Contraindication
- 최소 3년 유지 가능한지?
- Routes of AIT
 - SCIT 중 제품 선택, 스케줄 선택
 - **Anaphylaxis** 응급 대처가 준비된 환경에서 숙련된 의료진의 주사
 - 매 투여 후 최소 **30분** 모니터링이 필수적
 - SLIT 중 선택 (제품에 따라 초기, 유지 용법 상이)

Thank you for listening!

