

Controverse: ITSL/ITSC
CONTRA:

ITA en 2015

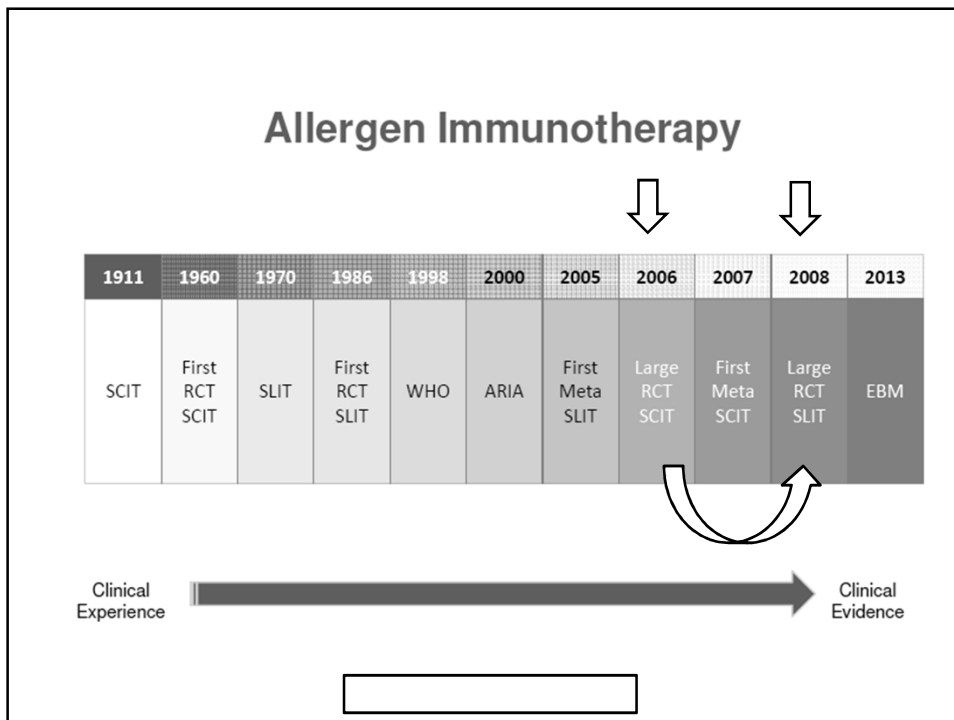
La sublinguale n'est pas la seule thérapeutique validée et praticable




Pneumo-allergologie pédiatrique
CHPLT de Verviers

Dr. Bénédicte Derkenne
Dr. Karin Giebels
Dr. Thierry Carvelli





Cochrane Database Syst Rev. 2007 Jan 24;(1):CD001936.

Allergen injection immunotherapy for seasonal allergic rhinitis.

Calderon MA¹, Alves B, Jacobson M, Hurwitz B, Sheikh A, Durham S.

AUTHORS' CONCLUSIONS: This review has shown that specific allergen injection immunotherapy in suitably selected patients with seasonal allergic rhinitis results in a significant reduction in symptom scores and medication use. Injection immunotherapy has a known and relatively low risk of severe adverse events. We found no long-term consequences from adverse events.

J Allergy Clin Immunol. 2001 Dec;108(6):921-8.

A double-blinded, comparative study of the effects of short pre-season specific immunotherapy and topical steroids in patients with allergic rhinoconjunctivitis and asthma.

Rak S¹, Heinrich C, Jacobsen L, Schevnius A, Venge P.

CONCLUSION: Treatment with NS was more effective than short-course pre-season SIT in reducing symptoms of rhinoconjunctivitis; however, the 2 therapies were equivalent in terms of the need for rescue medication. SIT prevented seasonal increase in bronchial hyperresponsiveness, eosinophil number, eosinophil cationic protein, and eosinophil chemotactic activity only in asthmatic patients. The mechanisms underlying bronchial hyperresponsiveness developing during allergen exposure in rhinitis might be different from those operating in asthma.

Norman Uptodate 2013

Clinical indications for allergen immunotherapy

Symptoms of allergic rhinitis, allergic conjunctivitis, allergic asthma, or any combination of these disorders after natural exposure to aeroallergens
AND
Demonstrable evidence of clinically relevant specific-IgE
AND
At least one of the following:
Poor response to pharmacotherapy, allergen avoidance, or both
Unacceptable adverse effects of medications
Wish to reduce or avoid long-term pharmacotherapy and the cost of medication
Coexisting allergic rhinitis and asthma
Possible prevention of asthma in patients with allergic rhinitis

Rostrum

Multiallergen immunotherapy for allergic rhinitis and asthma

Harold S. Nelson, MD *Denver, Colo*

allergens in the treatment regimen. It is concluded that simultaneous administration of more than 1 allergen extract is clinically effective. However, more studies are needed, particularly with more than 2 allergen extracts and with sublingual administration. (J Allergy Clin Immunol 2009;123:763-9.)

J Allergy Clin Immunol. 2012 Apr;129(4):929-34. doi: 10.1016/j.jaci.2011.11.019. Epub 2012 Jan 11.

Multiple-allergen and single-allergen immunotherapy strategies in polysensitized patients: looking at the published evidence.

Calderón MA¹, Cox L, Casale TB, Moingeon P, Demoly P.

Efficacy of subcutaneous and sublingual immunotherapy with grass allergens for seasonal allergic rhinitis: A meta-analysis-based comparison					
<small>J ALLERGY CLIN IMMUNOL NOVEMBER 2012</small>					
<small>Danilo Di Bona, MD, PhD,^{a,b,c} Antonella Plaia, PhD,^d Maria Stefania Leto-Barone, MD,^e Simona La Piana, MD,^a and</small>					
Evidence summary					
Systematic review	No. of RCTs	Symptom score	Medication score	Quality of life	Safety
Di Bona et al. [17*]	14 SCIT versus placebo	Pooled SMD for treatment effect:			Treatment-emerged AE:
	22 SLIT versus placebo	SCIT versus placebo: -0.92 (95% CI -1.26 to -0.58; P<0.0001)	SCIT versus placebo: -0.58; 95% CI -0.86 to -0.30		SCIT: 0.86 AEs/patient
	36 RCT 3000 patients Comparison indirecte	SLIT-D versus placebo: -0.25 (95% CI -0.45 to -0.05; P<0.01)	SLIT-D versus placebo: -0.37; 95% CI -0.7 to -0.00		SLIT: 2.13 AEs/patient
		SLIT-T versus placebo: -0.40 (95% CI -0.54 to -0.27; P<0.001)	SLIT-T versus placebo: -0.30; 95% CI -0.44 to -0.16		Anaphylaxis (episodes):

Efficacy of subcutaneous and sublingual immunotherapy with grass allergens for seasonal allergic rhinitis: A meta-analysis-based comparison					
<small>J ALLERGY CLIN IMMUNOL NOVEMBER 2012</small>					
<small>Danilo Di Bona, MD, PhD,^{a,b,c} Antonella Plaia, PhD,^d Maria Stefania Leto-Barone, MD,^e Simona La Piana, MD,^a and</small>					
Evidence summary					
Systematic review	No. of RCTs	Symptom score	Medication score	Quality of life	Safety
Di Bona et al. [17*]	14 SCIT versus placebo	Pooled SMD for treatment effect:			Treatment-emerged AE:
	22 SLIT versus placebo	SCIT versus placebo: -0.92 (95% CI -1.26 to -0.58; P<0.0001)	SCIT versus placebo: -0.58; 95% CI -0.86 to -0.30		SCIT: 0.86 AEs/patient
	36 RCT				
Conclusions: Our results provide indirect but solid evidence that SCIT is more effective than SLIT in controlling symptoms and in reducing the use of antiallergic medications in seasonal allergic rhinoconjunctivitis to grass pollen. (J Allergy Clin Immunol 2012;130:1097-107.)					
		-0.40 (95% CI -0.54 to -0.27; P<0.001)	95% CI -0.44 to -0.16		

Systematic review	No. of RCTs	Evidence summary			
		Symptom score	Medication score	Quality of life	Safety
Di Bona <i>et al.</i> [17*] 2012	14 SCIT versus placebo	Pooled SMD for treatment effect:			Treatment-emergent AE:
	22 SLIT versus placebo	SCIT versus placebo: -0.92 (95% CI -1.26 to -0.58; P<0.0001)	SCIT versus placebo: -0.58; 95% CI -0.86 to -0.30		SCIT: 0.86 AEs/patient
		SLIT-D versus placebo: -0.25 (95% CI -0.45 to -0.05; P<0.01)	SLIT-D versus placebo: -0.37; 95% CI -0.7 to -0.00		SLIT: 2.13 AEs/patient
		SLIT-T versus placebo: -0.40 (95% CI -0.54 to -0.27; P<0.001)	SLIT-T versus placebo: -0.30; 95% CI -0.44 to -0.16		Anaphylaxis (episodes): SCIT/SLIT: 12/1
Dretzke <i>et al.</i> [18*] 2013	17 SCIT versus placebo	SSD:	SSD:	SSD:	NR
	11 SLIT versus placebo (update to Cochrane Review)	SCIT versus SLIT: 0.351 (95% CrI 0.127-0.586) favoring SCIT	SCIT versus SLIT: 0.273 (95% CrI 0.027-0.529) favoring SCIT	SCIT versus SLIT: 0.383; 95% CrI, -0.042 to 0.804, P=NS) favoring SCIT	
Chelladurai <i>et al.</i> [19*] 2013	8 SCIT versus SLIT	Moderate-grade evidence favoring SCIT	Low grade evidence- no difference in treatment effectiveness between SCIT and SLIT	NR	Local reactions (frequency): SCIT: 20% SLIT: 6.7-56% Anaphylaxis (episodes) SCIT: 1 SLIT: 0
Kim <i>et al.</i> [20*]	3 SCIT versus SLIT (pediatrics only)	Low-grade evidence favoring SCIT	Low grade evidence favoring SCIT	NR	Local reactions (patients): SCIT: 3 SLIT: 3 Systemic reactions (patients): SCIT: 4 SLIT: 0 Anaphylaxis (episodes) SCIT: 1 SLIT: 0

SCIT/SLIT pour le traitement de la rhinite allergique

Take home messages

Pour les traitements disponibles actuellement en pharmacie

- **Efficacité**

- Rhinite allergique

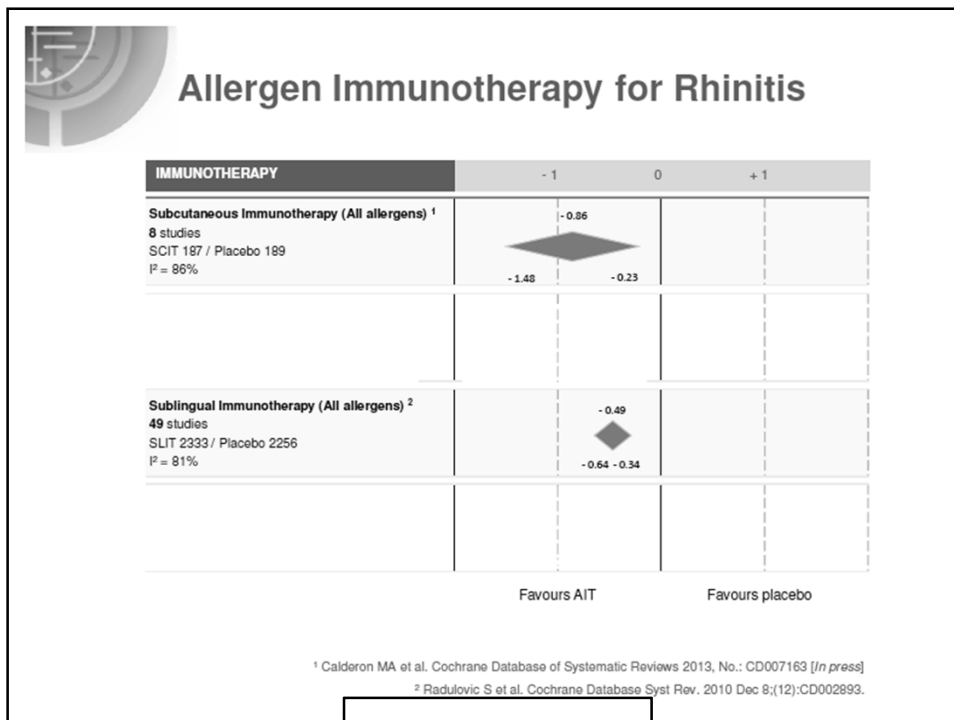
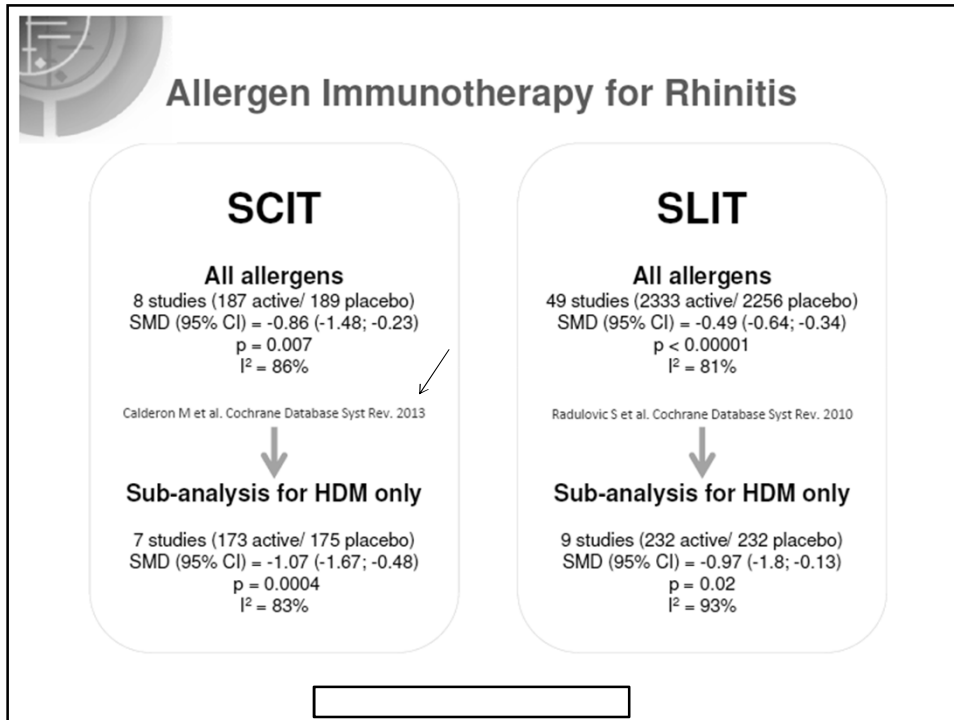
- Plus de bénéfice pour la SCIT chez l'adulte et chez l'enfant

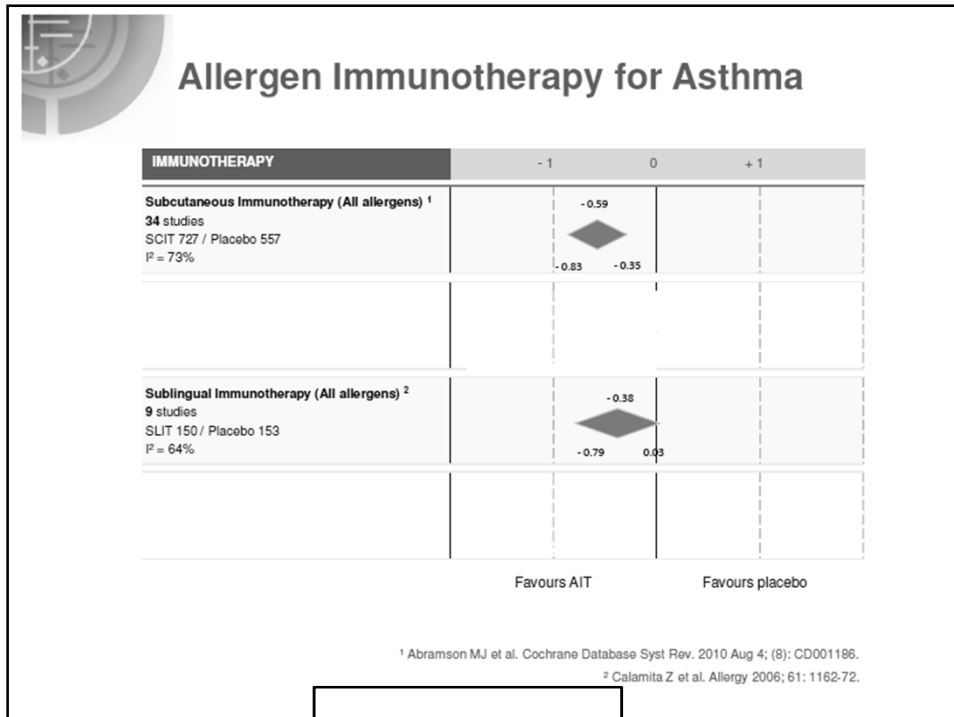
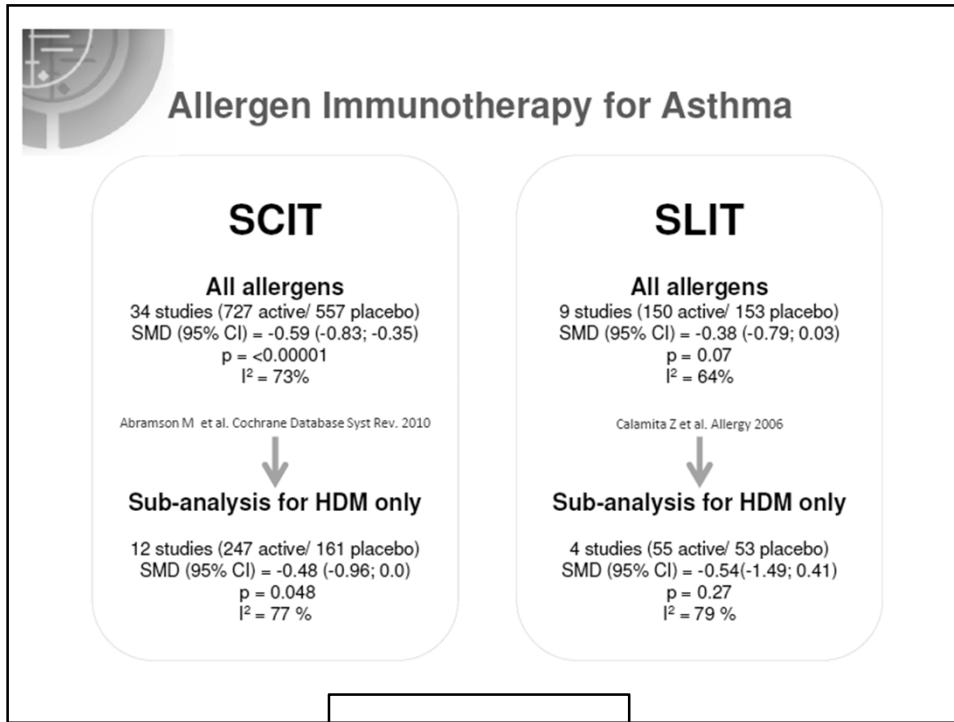
- Di Bona JACI 2012 (et toutes les autres revues moins rigoureuses)
 - » 36 RCT, 3000 patients
 - » comparaisons indirectes et hétérogénéités
 - » pas de comparaison les dernières SLIT comprimés (>2012)

- 2/3 études de comparaison **directe** SCIT/SLIT

- » Faible effectif

- Quirino CEA 1996: 20 adultes, graminées: SCIT>SLIT
- Khinchi Allergy 2004: 58 adultes bouleau: SCIT=SLIT
- Yukselen IAAI 2012 30 enfants, acariens+
 - SCIT amélioration de la rhinite et de l'asthme >>SLIT
 - Manque d'étude solide de comparaison directe SCIT/SLIT





Abramson 2003
 Cochrane Database Syst Rev. 2010 Aug 4;(8):CD001186. doi: 10.1002/14651858.CD001186.pub2.

Injection allergen immunotherapy for asthma.

MAIN RESULTS: Eighty-eight trials were included (13 new trials). There were 42 trials of immunotherapy for house mite allergy, 27 pollen allergy trials, 10 animal dander allergy trials; two Cladosporium mould allergy, two latex and six trials looking at multiple allergens. Concealment of allocation was assessed as clearly adequate in only 16 of these trials. Significant heterogeneity was present in a number of comparisons. Overall, there was a

AUTHORS' CONCLUSIONS: Immunotherapy reduces asthma symptoms and use of asthma medications and improves bronchial hyper-reactivity. One trial found that the size of the benefit is possibly comparable to inhaled steroids. The possibility of local or systemic adverse effects (such as anaphylaxis) must be considered.

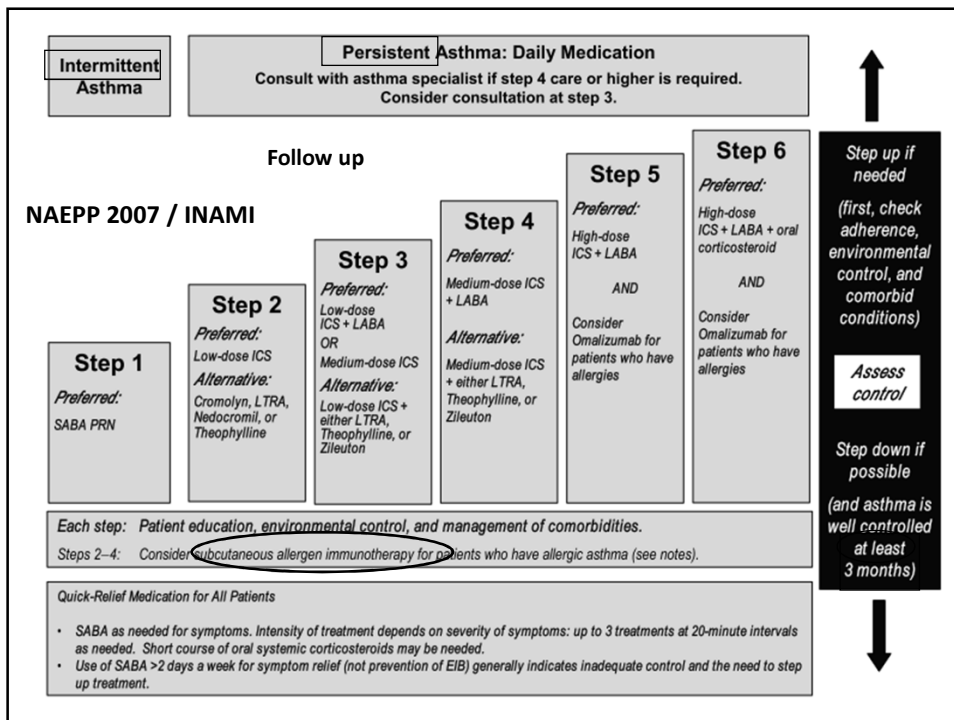
Après 2 ans: Fluticazone 330 à 151 290 à 206 µg

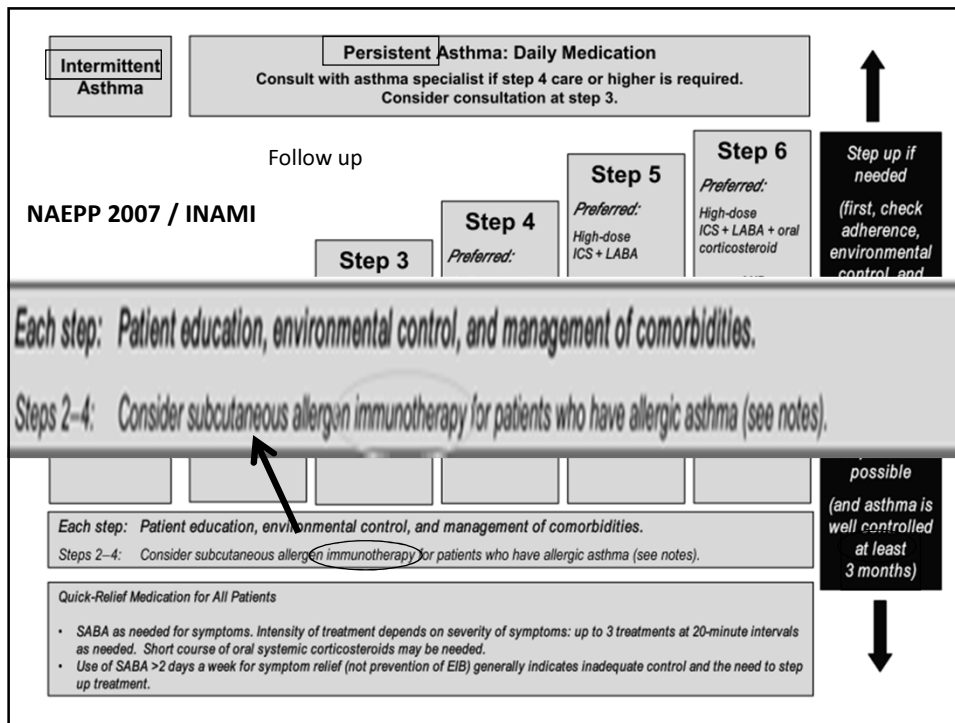
Steroid-sparing effects with allergen-specific immunotherapy in children with asthma: A randomized controlled trial
 RCT 65 enfants
 JACI 2010


Stefan Ziegen, MD,¹ Peter Karlos, MD,² and Enzo Medonini, MD³ Frankfurt, Germany, and Milan, Italy

Dose Step	SCIT + ICS (%)	ICS only (%)
-3	30	15
-2	18	3
-1	28	38
0	10	28
+1	6	10
+2	10	4
+3	0	4

Conclusion: Adding a mite allergoid SCIT to pharmacologic treatment is an effective and safe strategy to reduce







CHEST

Original Research

ASTHMA

Metaanalysis of the Efficacy of Sublingual Immunotherapy in the Treatment of Allergic Asthma in Pediatric Patients, 3 to 18 Years of Age*

Martin Penagos, MD, MSc; Giovanni Passalacqua, MD; Enrico Compalati, MD; Carlos E. Baena-Cagnani, MD; Socorro Orozco, MD; Alvaro Pedroza, MD; and Giorgio Walter Canonica, MD

9 /73 études acceptées: 441 patients
Pollinoses: olivier, graminée, mélange pollen G/B...,
Acarions

(CHEST 2008; 133:599 – 609)

les enfant souffrant d'asthme

Background: Recent studies have documented the efficacy and safety of sublingual immunotherapy (SLIT) in patients with rhinitis, but the value of this treatment in those with asthma is still debated. We evaluated the efficacy of SLIT in the treatment of allergic asthma in children by a metaanalysis of randomized, double-blind, and placebo-controlled (DBPC) clinical trials.

Methods: Electronic databases were searched up to May 31, 2006, for randomized DBPC trials assessing SLIT in pediatric cases of asthma. Effects on primary outcomes (*ie*, symptom scores and concomitant use of rescue medication) were calculated with standardized mean differences (SMDs) using the random-effects model. We performed the metaanalysis using a statistical software package (RevMan, 4.2.8; The Cochrane Collaboration; Oxford, UK), and we followed the recommendations of the Cochrane Collaboration and the Quality of Reporting of Metaanalyses guidelines.

Results: Seventy-three articles were identified and reviewed. Nine studies, all published after 1990, fulfilled the selection criteria. A total of 441 patients had a final assessment and were included in the analysis. Two hundred thirty-two patients received SLIT, and 209 patients received placebo. The results of the present analysis demonstrated a relevant heterogeneity due to widely differing scoring systems. Overall, there was a significant reduction in both symptoms (SMD - 1.14; 95% confidence interval [CI], - 2.10 to - 0.18; $p = 0.02$) and medication use (SMD, - 1.63; 95% CI, - 2.83 to - 0.44; $p = 0.007$) following SLIT.

Conclusion: SLIT with standardized extracts reduces both symptom scores and rescue medication use in children with allergic asthma compared with placebo. (CHEST 2008; 133:599-609)

les enfant souffrant d'asthme

Background: Recent studies have documented the efficacy and safety of sublingual immunotherapy (SLIT) in patients with rhinitis, but the value of this treatment in those with asthma is still debated. We evaluated the efficacy of SLIT in the treatment of allergic asthma in children by a metaanalysis of randomized, double-blind, and placebo-controlled (DBPC) clinical trials.

Methods: Electronic databases were searched up to May 31, 2006, for randomized DBPC trials assessing SLIT in pediatric cases of asthma. Effects on primary outcomes (*ie*, symptom scores and concomitant use of rescue medication) were calculated with standardized mean differences (SMDs) using the random-effects model. We performed the metaanalysis using a statistical software package (RevMan, 4.2.8; The Cochrane Collaboration; Oxford, UK), and we followed the recommendations of the Cochrane Collaboration and the Quality of Reporting of Metaanalyses guidelines.

Results: Seventy-three articles were identified and reviewed. Nine studies, all published after 1990, fulfilled the selection criteria. A total of 441 patients had a final assessment and were

Conclusion: SLIT with standardized extracts reduces both symptom scores and rescue medication use in children with allergic asthma compared with placebo. (CHEST 2008; 133:599-609)

use in children with allergic asthma compared with placebo. (CHEST 2008; 133:599-609)

Allergy 2006; 61: 185–190 **R. Dahl¹, A. Stender², S. Rak³** Copyright © Blackwell Munksgaard 2005
 ALLERGY
 DOI: 10.1111/j.1398-9995.2005.00949.x

Original article 114 patients 18-65 ans, asthme léger à modéré persistant: Grazax -10/14 sem
Specific immunotherapy with SQ standardized grass allergen tablets in asthmatics with rhinoconjunctivitis

Table 3. Average daily asthma medication and symptom score

Treatment group analysis set	Preseason		Grass pollen season	
	Placebo FAS (N = 40)	75 000 SQ-T FAS (N = 73)	Placebo FAS (N = 39)*	75 000 SQ-T FAS (N = 68)*
Asthma medication score				
Mean (SD)	0.09 (0.14)	0.09 (0.23)	0.66 (1.08)	0.71 (1.28)
Median	0.00	0.00	0.07	0.00
Minimum–maximum	0.00–0.49	0.00–1.35	0.00–4.00	0.00–5.33
Asthma symptom score				
Mean (SD)	0.33 (0.33)	0.23 (0.34)	0.74 (0.92)	0.44 (0.68)
Median	0.23	0.10	0.36	0.18
Minimum–maximum	0.00–1.05	0.00–2.00	0.00–3.60	0.00–3.67

*Number of subjects with seasonal diary data were 39 placebo and 68 active. FAS, full analysis set.

Results: Differences in asthma medication and symptom scores between the treatment groups were negligible. The mean difference in asthma medication score was below 0.1 and 0.3 for asthma symptom score [a single inhalation of salbutamol (200 µg) was scored 2]. No serious adverse events were reported. A reduction in rhinoconjunctivitis symptom score of 37% ($P = 0.004$) and a 41% ($P = 0.036$) reduction in medication score was found in the grass pollen season for subjects treated with the grass allergen tablet compared with placebo. Well days increased by 54% ($P = 0.002$).

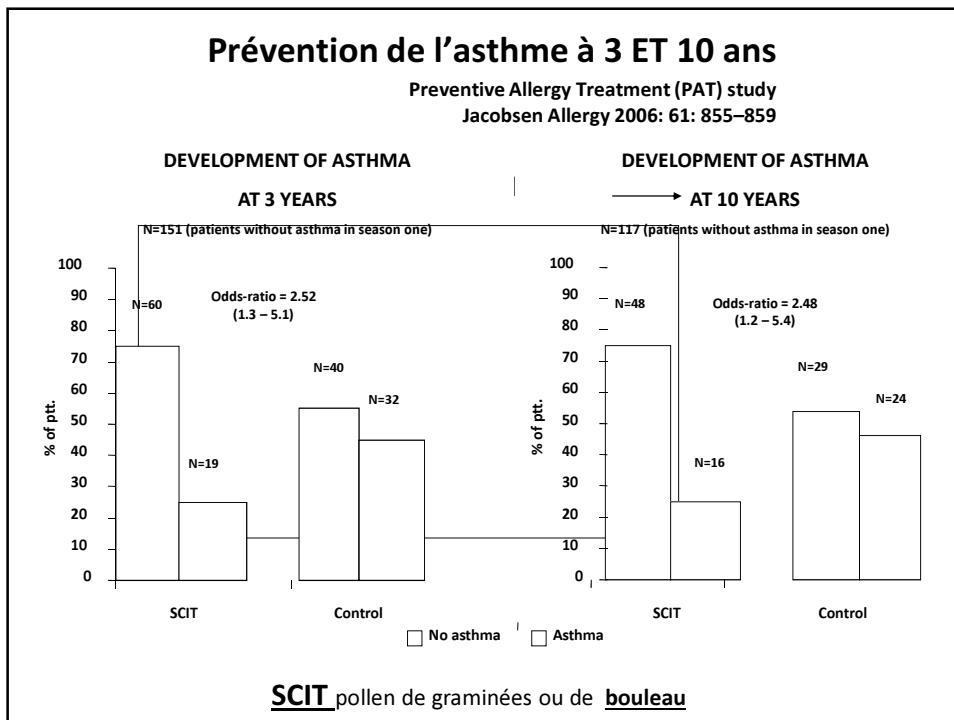
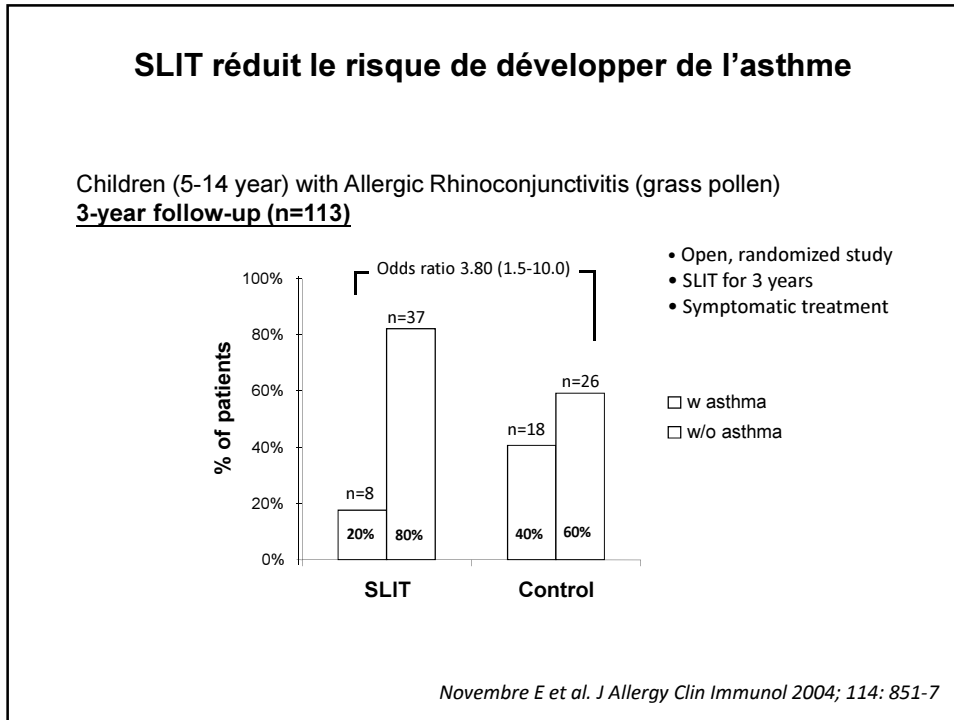
Original Article J ALLERGY CLIN IMMUNOL: IN PRACTICE
 JULY/AUGUST 2013

Effectiveness of Subcutaneous Versus Sublingual Immunotherapy for the Treatment of Allergic Rhinoconjunctivitis and Asthma: A Systematic Review

Yohalakshmi Chelladurai, MBBS, MPH*, Catalina Suarez-Cuervo, MD*, Nkiruka Erekosima, MD, MPH*, Julia M. Kim, MD, MPH*, Murugappan Ramanathan, MD*, Jodi B. Segal, MD, MPH*, and Sandra Y. Lin, MD*
 Baltimore, Md

RESULTS: Eight trials compared the effectiveness and safety of SCIT and SLIT. The effectiveness of the 2 forms of immunotherapy in managing allergic asthma and rhinoconjunctivitis were reported in 4 and 6 clinical trials, respectively. Low-grade evidence supports greater effectiveness of SCIT than SLIT for asthma symptom reduction and also at reducing a combined measure of rhinitis symptoms and medication use. Moderate-grade evidence supports greater effectiveness of SCIT than SLIT for nasal and/or eye symptom reduction. All 8 trials reported on adverse events with an episode of anaphylaxis reported in a child treated with SCIT.

CONCLUSION: Our review provides low-grade evidence to support that SCIT is superior to SLIT for reduction in asthma symptoms and moderate-grade evidence for reduction of allergic rhinoconjunctivitis. Additional studies are required to strengthen this evidence base for clinical decision making. © 2013 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol: In Practice 2013;1:361-9)



Take home messages

Pour les traitements disponibles actuellement en pharmacie

- Efficacité (SCIT NR: aliments, médicaments, latex s. oral)
 - Allergie au venin d’hyménoptères
 - Rhinite allergique
 - Plus de bénéfice pour la SCIT chez l’adulte et chez l’enfant
 - Di Bona JACI 2012 (et toutes les autres revues moins rigoureuses)
 - » 36 RCT, 3000 patients
 - » comparaisons indirectes et hétérogénéités
 - » pas de comparaison les dernières SLIT comprimés (>2012)
 - 2/3 études de comparaison directe SCIT/SLIT
 - » Faible effectif
 - Quirino CEA 1996+, Khinchi Allergy 2004-, Yukselen IAAI 2012+
 - - Plus d’allergènes **validés** pour la SCIT que pour la SLIT
 - » SCIT: acariens, bouleau graminées, cèdre de montagne amброisie, pariétaire, ép. chat et chien, alternaria, cladosporium, blatte
 - » SLIT: acariens, graminée, bouleau, amброisie
 - Asthme allergique méta analyses disponibles
 - Enfant efficacité validée pour SLIT et SCIT
 - Adulte efficacité validée pour SCIT
 - SCIT durée optimale 3 ans (Des Roches Allergy 1996, Tabar JACI 2011)
 - SLIT 4 ans Marogna JACI 2010
 - Prévention **à 10 ans** de l’asthme chez la patient souffrant de rhinite allergique
 - Seule la SCIT dispose d’études rigoureuses et robuste validant cette indication
 - Indic.: 1. RA 2. traitement chronique 3. AH asthme 4. Volonté parentale de prévention
 - Durabilité de l’effet protecteur selon le schéma
 - Seules les SLIT en comprimés ont encadré la dose optimale mais leur recul n’est que de 5 ans

Efficacy of subcutaneous and sublingual immunotherapy with grass allergens for seasonal allergic rhinitis: A meta-analysis-based comparison J ALLERGY CLIN IMMUNOL NOVEMBER 2012

Danilo Di Bona, MD, PhD,^{a,b,c} Antonella Plaia, PhD,^d Maria Stefania Leto-Barone, MD,^e Simona La Piana, MD,^e and

Systematic review	No. of RCTs	Evidence summary			
		Symptom score	Medication score	Quality of life	Safety
Di Bona et al. [17*] 36 RCT 3000 patients Comparaison indirecte	14 SCIT versus placebo	Pooled SMD for treatment effect:			Treatment-emerged AE:
	22 SLIT versus placebo	SCIT versus placebo: -0.92 (95% CI -1.26 to -0.58; P<0.0001)	SCIT versus placebo: -0.58; 95% CI -0.86 to -0.30		SCIT: 0.86 AEs/patient
	SLIT-D versus placebo: -0.25 (95% CI -0.45 to -0.05; P<0.01)	SLIT-D versus placebo: -0.37; 95% CI -0.7 to -0.00		SLIT: 2.13 AEs/patient	
	SLIT-T versus placebo: -0.40 (95% CI -0.54 to -0.27; P<0.001)	SLIT-T versus placebo: -0.30; 95% CI -0.44 to -0.16		Anaphylaxis (episodes):	

Efficacy of subcutaneous and sublingual immunotherapy with grass allergens for seasonal allergic rhinitis: A meta-analysis-based comparison

Daniilo Di Bona, MD, PhD,^{a,b,c} Antonella Plaia, PhD,^d Maria Stefania Leto-Barone, MD,^e Simona La Piana, MD,^g and

TABLE II. Total AEs related to SCIT and SLIT

	SCIT		SLIT	
	Treated	Placebo	Treated	Placebo
Total AEs, no.	960	456	4046	1856
Total AEs/patients, %	0.86	0.5	2.13	0.99
Withdrawals for AE, no.	18	5	78	25
Withdrawals for AE/patient, %	0.019	0.005	0.04	0.013
Anaphylactic reactions, no. (adrenaline)	12	2	1	0
	1,25%	0,4%	0,02%	

← 32%

Conclusions: Our results provide indirect but solid evidence that SCIT is more effective than SLIT in controlling symptoms and in reducing the use of antiallergic medications in seasonal allergic rhinoconjunctivitis to grass pollen. (J Allergy Clin Immunol 2012;130:1097-107.)

SLIT induced-anaphylaxis - Published case-reports

1. Anaphylaxis to sublingual immunotherapy. *Dunsky EH. et al. Allergy 2006 ; 61 : 1235*
A poorly described case-report – mixture of 6 allergens (probably not standardized)
2. Anaphylaxis by latex sublingual immunotherapy. *Antico A. et al. Allergy 2006 ; 61 : 1236-37*
Latex is not commonly used for SLIT + rush protocol
3. Anaphylaxis to multiple pollen allergen sublingual immunotherapy (Staloral) *Eifan AO. et al. Allergy 2007; 62 : 567- 68*
A severe local adverse reaction not an anaphylactic shock
4. Anaphylactic shock because of sublingual immunotherapy (Staloral) overdose during third year of maintenance dose. *Blazowski I. Allergy 2008; 63:374*
After a long period of SLIT cessation the patient restarted with a very high dose without medical supervision
5. Anaphylactic reaction after the first dose of sublingual immunotherapy with grass pollen tablet (Grazax). *de Groot H., Bijl A. Allergy 2009: 64: 961-967*
Two anaphylactic reactions after first dose of grass pollen tablet, resulting in a strict advice to take the first tablet under medical observation.

Efficacy of subcutaneous and sublingual immunotherapy with grass allergens for seasonal allergic rhinitis: A meta-analysis-based comparison

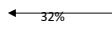
Danilo Di Bona, MD, PhD,^{a,b,c} Antonella Plaia, PhD,^d Maria Stefania Leto-Barone, MD,^e Simona La Piana, MD,^e and

TABLE II. Total AEs related to SCIT and SLIT

	SCIT		SLIT	
	Treated	Placebo	Treated	Placebo
Total AEs, no.	960	456	4046	1856
Total AEs/patients, %	0.86	0.5	2.13	0.99
Withdrawals for AE, no.	18	5	78	25
Withdrawals for AE/patient, %	0.019	0.005	0.04	0.013
Anaphylactic reactions, no. (adrenaline)	12	2	1	0

Epstein JACI 2014

1,25% 0,4% 0,02%



SCIT entre 2008 et 2012

Sur 23,3 million d'injections : 1 décès en 2009

FR: -asthme symptomatique

- degré de sensibilité à l'allergène, B bloquants,
- nouveau flacon, pic de pollinisation, erreur de dose

REVIEW ARTICLE

Systematic reviews of sublingual immunotherapy (SLIT)

S. Radulovic¹, D. Wilson², M. Calderon³ & S. Durham³

¹Paediatric Allergy, King's College, London; ²Selly Oak Hospital, University Hospitals Birmingham NHS Trust, Birmingham, UK; ³Royal Brompton Hospital, Upper Respiratory Medicine, London, UK

P < 0.00001)) compared with placebo. None of the trials reported severe systemic reactions, anaphylaxis or use of Adrenaline. This updated review reinforces the conclusion of the original 2003 Cochrane Review that sublingual immunotherapy is effective for allergic rhinitis and appears a safe route of administration.

analysis. We used standardised mean difference (SMD), with a random effect model

SIT (Abramson Cochrane review 2003)
 Réaction allergique généralisée 1/1250 à 1/2206
 Near fatal 5,4 /1 million
 Décès 1 à 2 /1 million
 FR: Asthme non contrôlé , VEMS < nle

Take home messages

- Sécurité
 - SLIT moins ES effet locaux+ et généraux-- que la SCIT
 - » Mais
 - SLIT: réactions anaphylactiques ont été décrites sous Grazax
 - La SLIT en comprimés doit être initiée sous supervision médicale
 - SLIT: effets secondaires même faibles peuvent être quotidiens et sans supervision médicale ce qui peu diminuer l'observance
 - SCIT: réactions anaphylactiques sévères mettant la vie du patient en danger
 - 1 à 5 /millions (Abramson 2003) 1 décès/23 10⁶ i (Epstein 2014)
 - UE mortalité par accident de la route en 2013
 - 52/millions d'habitants (65 en Belgique)
 - Asthme instable, VEMS< nl
 - Patients détectables donc prévention possible
- Contre-indications (=SLIT):
 - Asthme sévère, instable
 - » corticothérapie orale, hospi ou intubé pour CA<6 mois, VEMS<75%,
 - » Anti IGE avant initiation chez ces patients ?
 - Beta bloquant
 - Mal. auto-immunitaire, HIV
 - Pas de critère d'âge > 60 ans
 - » comorbidité
 - Pas d'initiation durant la grossesse

Efficacy of subcutaneous and sublingual immunotherapy with grass allergens for seasonal allergic rhinitis: A meta-analysis-based comparison

Danilo Di Bona, MD, PhD,^{a,b,c} Antonella Plaia, PhD,^d Maria Stefania Leto-Barone, MD,^e Simona La Piana, MD,^a and

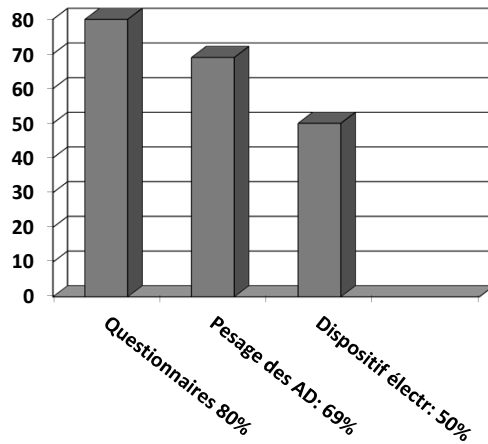
TABLE II. Total AEs related to SCIT and SLIT

	SCIT		SLIT	
	Treated	Placebo	Treated	Placebo
Total AEs, no.	960	456	4046	1856
Total AEs/patients, %	0.86	0.5	2.13	0.99
Withdrawals for AE, no.	18	5	78	25
Withdrawals for AE/patient, %	0.019	0.005	0.04	0.013
Anaphylactic reactions, no. (adrenaline)	12	2	1	0
	1,25%	0,4%	0,02%	

← 32%

Conclusions: Our results provide indirect but solid evidence that SCIT is more effective than SLIT in controlling symptoms and in reducing the use of antiallergic medications in seasonal allergic rhinoconjunctivitis to grass pollen. (J Allergy Clin Immunol 2012;130:1097-107.)

L' étude de Bender a étudié durant 6 mois l'observance d'enfants asthmatiques concernant la prise de corticoïdes inhalés simultanément selon trois méthodes de mesure différentes.



- Tendance à surestimer l'observance thérapeutique par les questionnaires.

Bender, BR; Wamboldt FR, O'Connor SH et al. - Measurement of children's asthma medication adherence by self report, mother report, canister weight, and Doser CT. Annals of Allergy, Asthma and Immunology, 2000, 85, 5,416-421.

Original Article
Early Compliance and Efficacy of Sublingual Immunotherapy in Patients with Allergic Rhinitis for House Dust Mites

Hyun Chang, MD¹ · Doo Hee Han, MD^{1,2} · Ji-hun Mo, MD¹ · Jeong-Whun Kim, MD^{1,2} · Dong-Young Kim, MD^{1,2}
 Chul Hee Lee, MD^{1,2} · Yang-Gi Min, MD^{1,2} · Chae-Seo Rhee, MD^{1,2,3}

- RA: Slit derm ptéron derm far 6-13 mois (9,8)
- Arrêt de Slit 31%
 - 58% <3 mois 22% <4-6 mois 19% >7 mois

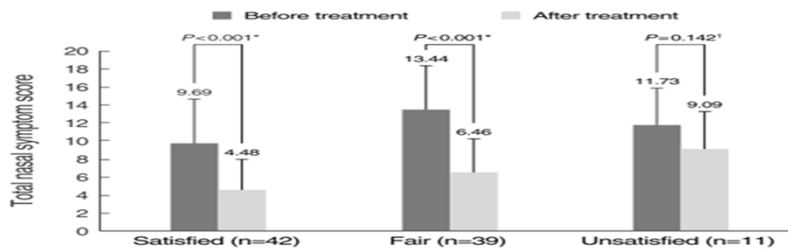


Fig. 2. Comparing the total nasal symptom scores (TNSSs) before and after sublingual immunotherapy (SLIT) in the satisfied, the fairly satisfied and the unsatisfied groups. The satisfied and the fairly satisfied group got better, with statistical significance. However, the TNSS of the unsatisfied group was not improved after SLIT.
 *statistical analysis using paired t-tests; †statistical analysis using the Wilcoxon signed rank test.

CEO *Clinical and Experimental Otorhinolaryngology* Vol. 2, No. 3: 136-140, September 2009 DOI 10.3342/ceo.2009.2.3.136
Original Article

Early Compliance and Efficacy of Sublingual Immunotherapy in Patients with Allergic Rhinitis for House Dust Mites

Hyun Chang, MD¹ · Doo Hee Han, MD^{1,2} · Ji-hun Mo, MD¹ · Jeong-Whun Kim, MD^{1,2} · Dong-Young Kim, MD^{1,2}
Chul Hee Lee, MD^{1,2} · Yang-Gi Min, MD^{1,2} · Chae-Seo Rhee, MD^{1,2,3}

- RA: Slit derm ptéron derm far 6-13 mois (9,8)
- Arrêt de Slit 31%
 - 58% <3 mois 22% <4-6 mois 19% >7 mois

Table 1. Adverse effects of sublingual immunotherapy

Adverse effects	Up-dosing phase ≥6 months	
Aggravation of symptoms	31 (33.7%)	7 (7.6%)
Itching sense of the oral cavity or insert the lip	9 (9.8%)	1 (1.1%)
Itching sense or discomfort of the eye	23 (25.0%)	3 (3.3%)
Skin itching or rash	15 (16.3%)	3 (3.3%)
Gastrointestinal trouble	14 (15.2%)	1 (1.1%)
Breathing discomfort	2 (2.2%)	5 (5.4%)
Wheezing	2 (2.2%)	0
The numbers are not mutually exclusive.	48%	12% ←

CEO *Clinical and Experimental Otorhinolaryngology* Vol. 2, No. 3: 136-140, September 2009 DOI 10.3342/ceo.2009.2.3.136
Original Article

Early Compliance and Efficacy of Sublingual Immunotherapy in Patients with Allergic Rhinitis for House Dust Mites

Hyun Chang, MD¹ · Doo Hee Han, MD^{1,2} · Ji-hun Mo, MD¹ · Jeong-Whun Kim, MD^{1,2} · Dong-Young Kim, MD^{1,2}
Chul Hee Lee, MD^{1,2} · Yang-Gi Min, MD^{1,2} · Chae-Seo Rhee, MD^{1,2,3}

- RA: Slit derm ptéron derm far 6-13 mois (9,8)
- Arrêt de Slit 31%
 - 58% <3 mois 22% <4-6 mois 19% >7 mois

Table 1. Adverse effects of sublingual immunotherapy

Adverse effects	Up-dosing phase ≥6 months	
Aggravation of symptoms	31 (33.7%)	7 (7.6%)
Itching sense of the oral cavity or insert the lip	9 (9.8%)	1 (1.1%)
Itching sense or discomfort of the eye	23 (25.0%)	3 (3.3%)
Skin itching or rash	15 (16.3%)	3 (3.3%)
Gastrointestinal trouble	14 (15.2%)	1 (1.1%)
Breathing discomfort	2 (2.2%)	5 (5.4%)
Wheezing	2 (2.2%)	0
The numbers are not mutually exclusive.	48%	12%

Original Article
Early Compliance and Efficacy of Sublingual Immunotherapy in Patients with Allergic Rhinitis for House Dust Mites
 Hyun Chang, MD¹ · Doo Hee Han, MD^{2*} · Ji-Hyun Mo, MD³ · Jeong-Wahn Kim, MD⁴ · Dong-Young Kim, MD⁵ · Chul Hye Lee, MD^{6*} · Yang-Gi Min, MD^{7*} · Chan-Seo Fhree, MD^{8*}

Arrêt de Slit 31%
 58% <3 mois 22% <4-6 mois 19% >7 mois

Causes d'arrêt de SLIT ?

- Incapacité de prendre le traitement selon le schéma fourni: 27.8%
- Inefficacité: 22.2%
- Inconfort de devoir se rendre à l'hôpital régulièrement : 16.7%
- Effets secondaires 13.9%
 - Aggravation des symptômes 5,5%
 - Fièvre 3%
 - Troubles gastro-intestinaux 3%
 - Éruptions cutanées 3%
- Coût 5,5%
- Difficulté de stockage du produit 3%
- Grossesse 3%
 - SLIT= obligation d'
 - éducation du patient
 - école de la SLIT

www.observita.eu

SLIT observance ???

- HSU Int Forum Allergy Rhinol 2012 (USA)
 - Abandon du traitement 40% après 4 ans
- Vita, Allergy 2010
 - 300 enfants 6-16 ans
 - Visite /3 ou 6 ou 12 mois
 - Abandon /30 68 82%
- Pajno Ped Allergu Immunol 2012
 - 150 enfant 3 à 6 ans
 - 46% d'abandon après 3 mois
- Senna JACI 2010
 - Achat réel des prescriptions de SLIT
 - Année 1: 44%, A2: 28%, A3:13%
- Kiel JACI 2013 (rétrospective)
 - 6486 patient SCIT ou SLIT
 - Trois ans de traitement complet
 - SCIT 23% connu donc gérable, négociable par le médecin
 - SLIT 7% souvent inconnu du médecin, difficile à gérer

- **si peu d'observance pratique ... peu d'efficacité (sécurité ?) en real life ?**
- **la régularité du coaching médical augmente l'observance**

Take home messages

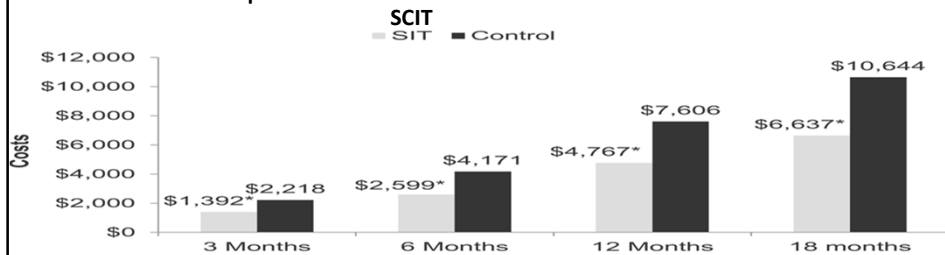
Pour les traitements disponibles actuellement en pharmacie

- **Confort du patient**
 - SLIT
 - Sous la langue à domicile
 - Mais quotidien 1 à 2 minutes x 30- 31 jours
 - Effet secondaire locaux parfois quotidiens
 - Rappel quotidien du fait d'être « malade » même en période asymptomatique
 - Pas à peu conseil/ coaching médical
 - observance??
 - SCIT
 - Injection SC mensuelle au cabinet du médecin/ personnel compétant 30 minutes/mois
 - Rappel mensuel du fait d'être « malade » même en période asymptomatique
 - Conseil/Coaching médical mensuel
 - observance
- **Contrôle de l'impact de l'observance sur l'efficacité du traitement**
 - SLIT: quasi impossible
 - SCIT: évident
 - Observance indispensable à l'efficacité et à la sécurité
 - Pour le traitement chronique cet observance est estimée à 50%
 - **SLIT: uniquement indiqué chez le patient probablement observant**
 - CI chez le patient inobservant pour les traitement classiques
- **Ecoles de l'ITA**
 - Quasi indispensables pour la SLIT
 - www.observita.eu

Allergy immunotherapy: Reduced health care costs in adults and children with allergic rhinitis

Cheryl S. Hankin, PhD,^a Linda Cox, MD,^b Amy Bronstone, PhD,^a and Zhaohui Wang, MS^a Moss Beach, Calif, and Fort Lauderdale-Davie, Fla

JACI 2013: 4997 patients suivis en Floride durant 18 mois Medicaid



J Allergy Clin Immunol. 2008 Jan;121(1):227-32. doi: 10.1016/j.jaci.2007.10.026.

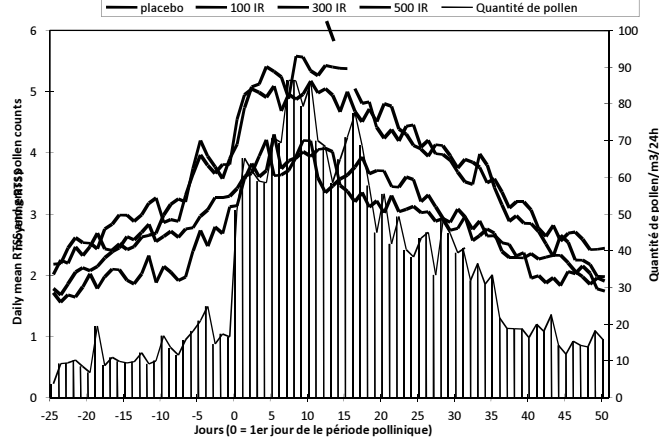
Allergy immunotherapy among Medicaid-enrolled children with allergic rhinitis: patterns of care, resource use, and costs.

Hankin CS¹, Cox L, Lang D, Levin A, Gross G, Eavy G, Meltzer E, Burgoyne D, Bronstone A, Wang Z.

CONCLUSION: Despite suboptimal treatment persistence (only 16% of patients completed 3 years of IT), resource use and costs after treatment were significantly reduced from pre-IT levels.

**5 Graminées dose optimale 300 IR/25 μ /ml
(Grazax 75000 SQ-T *Phleum pratense*)
300 IR également pour acariens, bouleau**

Figure 3: Moyenne quotidienne RTSS et niveau de pollen de graminée (2005)



➔ Efficacité significative pour les 300 IR et 500 IR, dès le 1er jour et tout au long de la saison pollinique, y compris au pic de pollen

Reference
Didier A. et al. JACI 2007

Take home messages

• Aspect financier pratique en Belgique pour le patient et sa famille

Frais non remboursés par l'INAMI

- Pour une ITA complète de trois ans
 - SLIT 300 IR/J
 - +- 1806 (Oralair 3 X 30, 7 mois /an) à 3240 euros (Stalloral Derm pteron derm far 12 mois /ans)
 - (+ 4 visites médicales: remboursement 13,52 x12=162 euros)
 - SCIT Kit de départ + 0,8 ml de 10I R/mois
 - +-270 euros (Alustal 5 graminées ou Derm ptéron derm far)
 - 13 sem induction+ 32 médicales/mois en 3 ans=45 cons x 13,52euro=608 euros
 - NB: rapport financier SCIT/SLIT fort comparable chez ALK mais Grazax X12/an ? ↑?
 - ITA non remboursée en Belgique
 - Possibilité d'activation du forfait vaccin <50 euros
 - Remboursement partiel (+-2/3) :
 - Mutualité neutre Verviers, Liège...
 - Mutualité libre des Canton de l'EST
 - Mutualité de chemins de fer (? 100%)
- Parfois ITA nécessaire chez trois enfants d'une même famille ...

En pratique

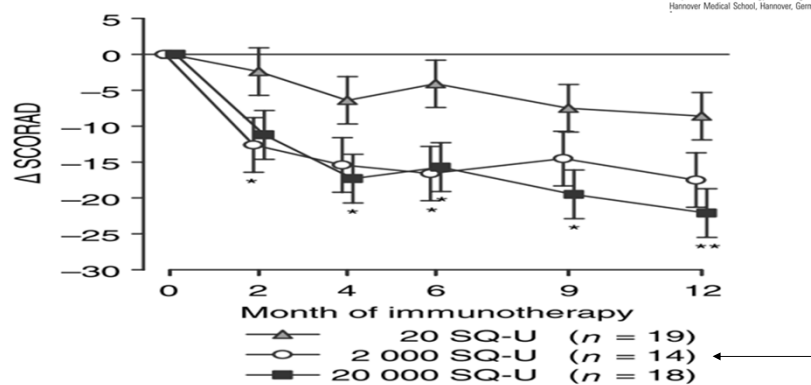
- **Mohamed 14 ans** (...+1 frère et 1 sœur)
 - Allergisation: Derm. Pteron. derm far.
 - Rhinite et asthme allergique modéré persistant
 - Habitation humide peu ventilée , 3 enfants/chambre
 - Revenu 2000 euros/mois
 - Echec des traitements classiques de la RA et de l' AA
 - **Justine 15 ans**
 - Allergisation à l'encontre des graminées
 - Rhinite et sinusite allergique invalidantes durant ses examens
 - Notion de fatigue sous AH
 - Inobservance++, ne se traite qu'en phase de décompensation
 - Parents prof. libérale divorcés avec garde alternée
 - **Florent 6 ans**
 - Allergisation à l'encontre des graminées
 - Rhinite et crises d'asthme de mai à août
 - Contrôle partiel sous AH, montelukast, CI, salbutamol
 - Parents asthmatiques motivés demandeur d'un amélioration durable
- Informer
 - Laisser le temps de réfléchir et de choisir en famille

Usefulness of specific immunotherapy in patients with atopic dermatitis and allergic sensitization to house dust mites: a multi-centre, randomized, dose-response study

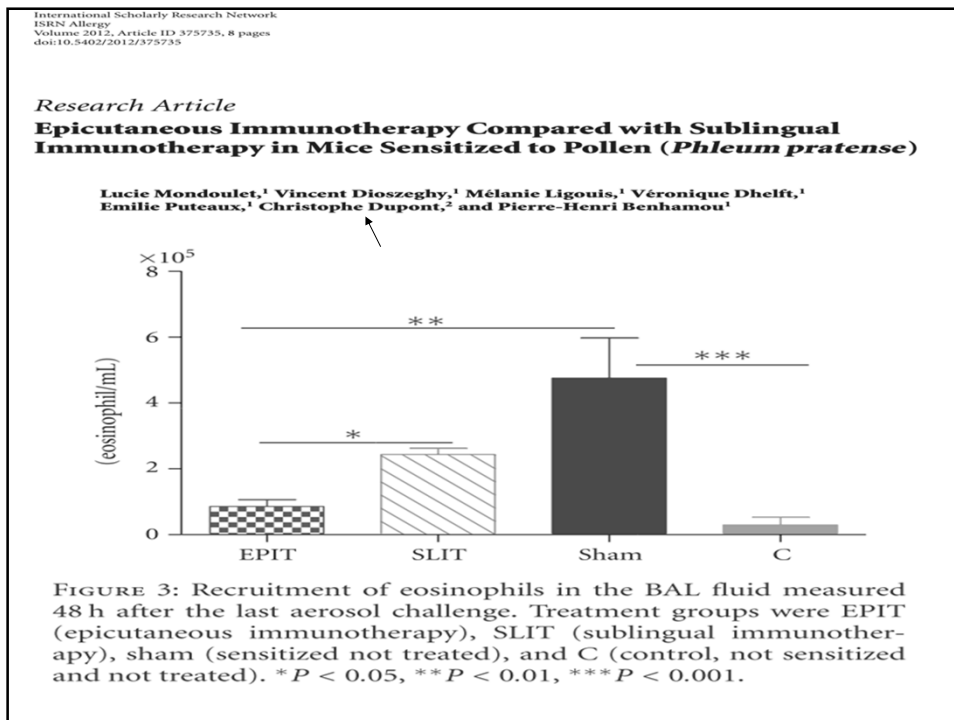
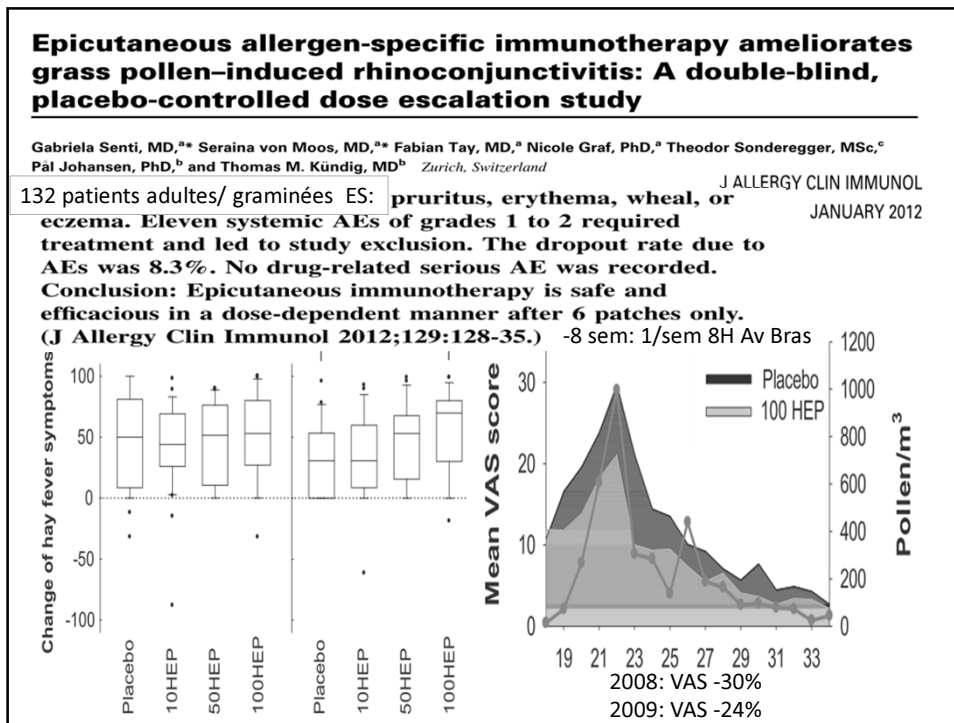
Allergy 2006; 61: 202-205

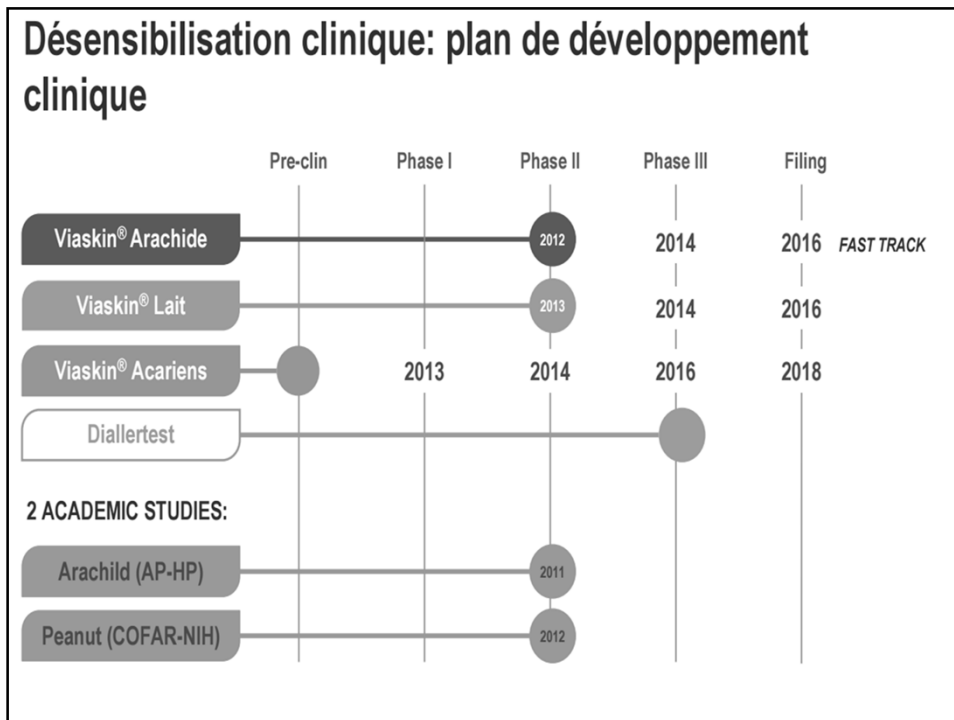
T. Werfel¹, K. Breuer¹, F. Rueff¹,
B. Przybilla¹, M. Worm¹, M. Grewa¹,
T. Ruzicka¹, R. Erhlich¹, H. Wolf¹,
J. Schnitker¹, A. Kapp¹

¹Department of Dermatology and Allergology,
Hanover Medical School, Hanover, Germany;



SCIT
Conclusions: Allergen-SIT for 1 year with a house dust mite preparation is able to improve the eczema in patients with atopic dermatitis who are sensitized to house dust mite allergens and reduces the need for topical corticosteroids. SIT may be valuable in the treatment of this chronic skin disease.





Intralymphatic immunotherapy

Senti and Kündig *World Allergy Organization Journal* (2015) 8:9
DOI 10.1186/s40413-014-0047-7

Abstract

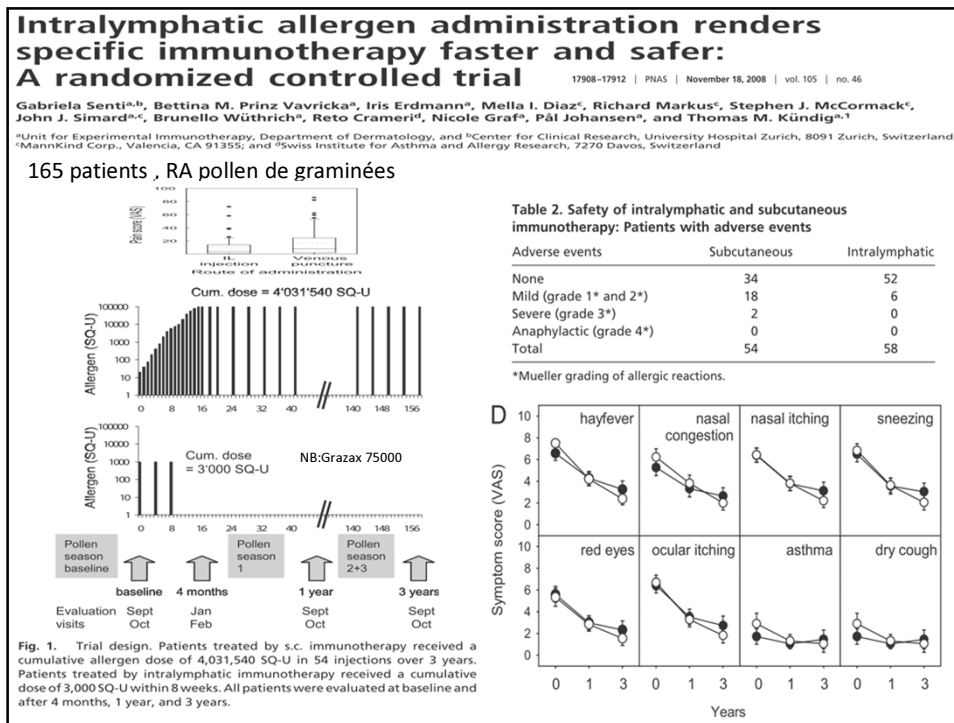
Gold Standard allergen-specific immunotherapy is associated with low efficacy because it requires either many subcutaneous injections of allergen or even more numerous sublingual allergen administrations to achieve amelioration of symptoms. Intralymphatic vaccination can maximize immunogenicity and hence efficacy. We and others have demonstrated that as few as three low dose intralymphatic allergen administrations are sufficient to effectively alleviate symptoms. Results of recent prospective and controlled trials suggest that this strategy may be an effective form of allergen immunotherapy.

Keywords: Administration routes, Allergen immunotherapy, Intralymphatic, Vaccination

Figure 1 Biodistribution after intralymphatic administration. Biodistribution of 99mTc-labelled human IgG after intralymphatic (left abdominal side) and subcutaneous (right abdominal side) injections. Radio tracing was made by gamma-imaging 20 min (left panel) and 25 hours (right panel) after injection. Arrows indicate the site of injection (s.c., subcutaneous, i.l., intralymphatic).

Figure 2 Intralymphatic injection. A sand blasted needle, being inserted into the lymph node from the right was used for better reflector and therefore visibility in the ultrasonid. The dark, hyperechoic area represents the periphery of the lymph node, which is approx. 15 mm long and 5 mm under the skin surface.

-Venin d'hyménoptères
-Graminées
.....?



Take home messages

Futur de l'ITA: SLIT, SCIT...EPIT, ILIT

- SCIT pour la dermatite atopique
- ITA par voie
 - épicutanée EPIT
 - » Graminées (Senti JACI 2012)
 - » Arachide, Lait de vache, acariens...
 - Intra lymphatique ILIT
- ITA utilisant
 - Allergènes recombinants
 - Allergène modifiés
 - Isoformes hypoallergéniques
 - Peptide tolérrogènes
 - Adjuvant
 - » Augmentation de l'efficacité
 - » Augmentation de la sécurité et de la tolérance

Take home messages

Pour les traitements disponibles actuellement en pharmacie

- Efficacité (SCIT NR: aliments, médicaments, latex s. oral)
 - Allergie au venin d'hyménoptères
 - Rhinite allergique
 - Plus de bénéfice pour la SCIT chez l'adulte et chez l'enfant
 - Di Bona JACI 2012 (et toutes les autres revues moins rigoureuses)
 - » 36 RCT, 3000 patients
 - » comparaisons indirectes et hétérogénéités
 - » pas de comparaison les dernières SLIT comprimés (>2012)
 - 2/3 études de comparaison directe SCIT/SLIT
 - » Faible effectif
 - Quirino CEA 1996+, Khinchi Allergy 2004-, Yukselen IAAI 2012+
 - Plus d'allergènes **validés** pour la SCIT que pour la SLIT
 - » SCIT: acariens, bouleau graminées, cèdre de montagne ambroisie, pariétaire, ép. chat et chien, alternaria, cladosporium, blatte
 - » SLIT: acariens, graminée, bouleau, ambroisie
 - Asthme allergique méta analyses disponibles
 - Enfant efficacité validée pour SLIT et SCIT
 - Adulte efficacité validée pour SCIT
 - SCIT durée optimale 3 ans (Des Roches Allergy 1996, Tabar JACI 2011)
 - SLIT 4 ans Marogna JACI 2010
 - Prévention **à 10 ans** de l'asthme chez la patient souffrant de rhinite allergique
 - Seule la SCIT dispose d'études rigoureuses et robuste validant cette indication
 - Indic.: 1. RA 2. traitement chronique 3. AH asthme 4. Volonté parente de prévention
 - Durabilité de l'effet protecteur selon le schéma
 - Seules les SLIT en comprimés ont encadré la dose optimale mais leur recul n'est que de 5 ans

Take home messages

- Sécurité
 - SLIT moins ES effet locaux+ et généraux-- que la SCIT
 - » Mais
 - SLIT: réactions anaphylactiques ont été décrites sous Grazax
 - La SLIT en comprimés doit être initiée sous supervision médicale
 - SLIT: effets secondaires même faibles peuvent être quotidiens et sans supervision médicale ce qui peu diminuer l'observance
 - SCIT: réactions anaphylactiques sévères mettant la vie du patient en danger
 - 1 à 5 /millions (Abramson 2003) 1 décès/23 10⁶ i (Epstein 2014)
 - UE mortalité par accident de la route en 2013
 - 52/millions d'habitants (65 en Belgique)
 - Asthme instable, VEMS< nl
 - Patients détectables donc prévention possible
 - Contre-indications (=SLIT):
 - Asthme sévère, instable
 - » corticothérapie orale, hospi ou intubé pour CA<6 mois, VEMS<75%,
 - » Anti IGE avant initiation chez ces patients ?
 - Beta bloquant
 - Mal. auto-immunitaire, HIV
 - Pas de critère d'âge > 60 ans
 - » comorbidité
 - Pas d'initiation durant la grossesse

Take home messages

Pour les traitements disponibles actuellement en pharmacie

- **Confort du patient**
 - SLIT
 - Sous la langue à domicile
 - Mais quotidien 1 à 2 minutes x 30- 31 jours
 - Effet secondaire locaux parfois quotidiens
 - Rappel quotidien du fait d'être « malade » même en période asymptomatique
 - Pas à peu conseil/ coaching médical
 - -observance??
 - SCIT
 - Injection SC mensuelle au cabinet du médecin/ personnel compétent 30 minutes/mois
 - Rappel mensuel du fait d'être « malade » même en période asymptomatique
 - Conseil/Coaching médical mensuel
 - +observance
- **Contrôle de l'impact de l'observance sur l'efficacité du traitement**
 - SLIT: quasi impossible
 - SCIT: évident
 - Observance indispensable à l'efficacité et à la sécurité
 - Pour le traitement chronique cet observance est estimée à 50%
 - **SLIT: uniquement indiqué chez le patient probablement observant**
 - CI chez le patient inobservant pour les traitement classiques
- **Ecoles de l'ITA**
 - Quasi indispensables pour la SLIT
 - www.observita.eu

Take home messages

Aspect financier pratique en Belgique pour le patient et sa famille

Frais non remboursés par l'INAMI

- Pour une ITA complète de trois ans
 - SLIT 300 IR/J
 - +- 1806 (Oralair 3 X 30, 7 mois /an) à 3240 euros (Stalloral Derm pteron derm far 12 mois /ans)
 - (+ 4 visites médicales: remboursement 13,52 x12=162 euros)
 - SCIT Kit de départ + 0,8 ml de 10I R/mois
 - +-270 euros (Alustal 5 graminées ou Derm ptéron derm far)
 - 13 sem induction+ 32 médicales/mois en 3 ans=45 cons x 13,52euro=608 euros
 - NB: rapport financier SCIT/SLIT fort comparable chez ALK mais Grazax X12/an ? ↑?
 - ITA non remboursée en Belgique
 - Possibilité d'activation du forfait vaccin <50 euros
 - Remboursement partiel (+-2/3) :
 - Mutualité neutre Verviers, Liège...
 - Mutualité libre des Canton de l'EST
 - Mutualité de chemins de fer (? 100%)
- Parfois ITA nécessaire chez trois enfants d'une même famille ...

Take home messages
Futur de l'ITA: SLIT, SCIT...EPIT, ILIT

- SCIT pour la dermatite atopique
- ITA par voie
 - épicutanée EPIT
 - » Graminées (Senti JACI 2012)
 - » Arachide ,Lait de vache, acariens...
 - **Intra lymphatique ILIT**
- ITA utilisant
 - Allergènes recombinants
 - Allergène modifiés
 - Isoformes hypoallergéniques
 - Peptide tolérogènes
 - Adjuvant
 - » Augmentation de l'efficacité
 - » Augmentation de la sécurité et de la tolérance

ITA en 2015

La sublinguale n'est **et ne sera pas** pas la seule thérapeutique validée et praticable



Pneumo-allergologie pédiatrique
CHPLT de Verviers

Dr. Bénédicte Derkenne
Dr. Karin Giebels
Dr. Thierry Carvelli

ABEFORCAL
OMB

