

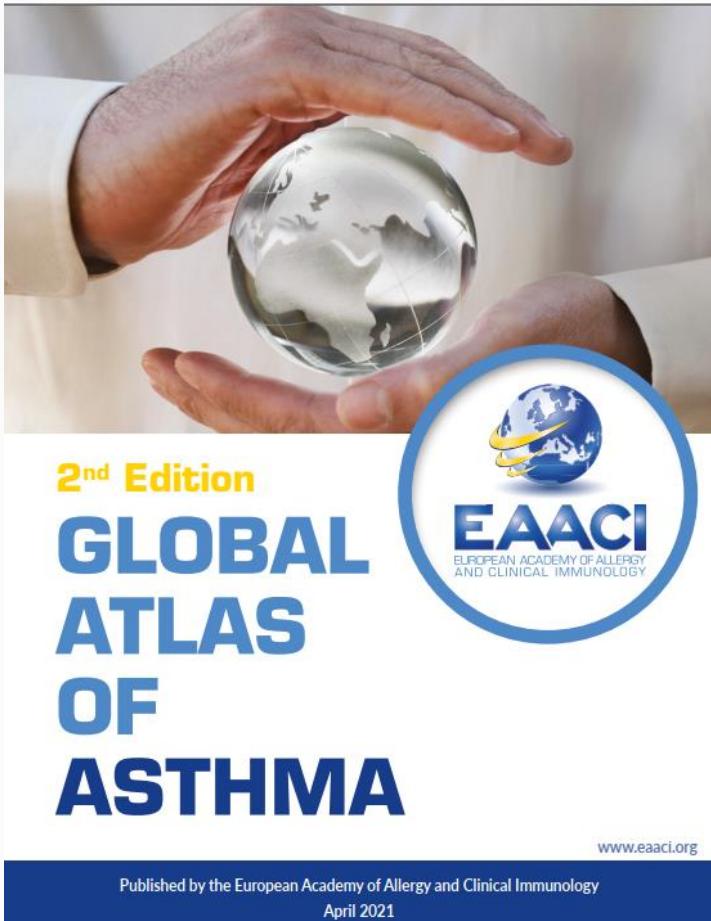


Spezifische Immuntherapie bei Patienten mit allergischem Asthma bronchiale

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Allergische Rhinitis



- 75%-90% der Patienten mit Asthma haben eine assoziierte Rhinitis
- 10-40% der Patienten mit allergischer Rhinitis (AR) haben ein Asthma
- AR in Asthma Patienten zu 30% unterdiagnostiziert
- Patienten mit AR Risiko für Asthma (OR 32)
- Moderate bis schwere allergische Rhinitis: Risikofaktor für unkontrolliertes Asthma (OR 13)



Klimek & Hagemann

Adults & adolescents 12+ years

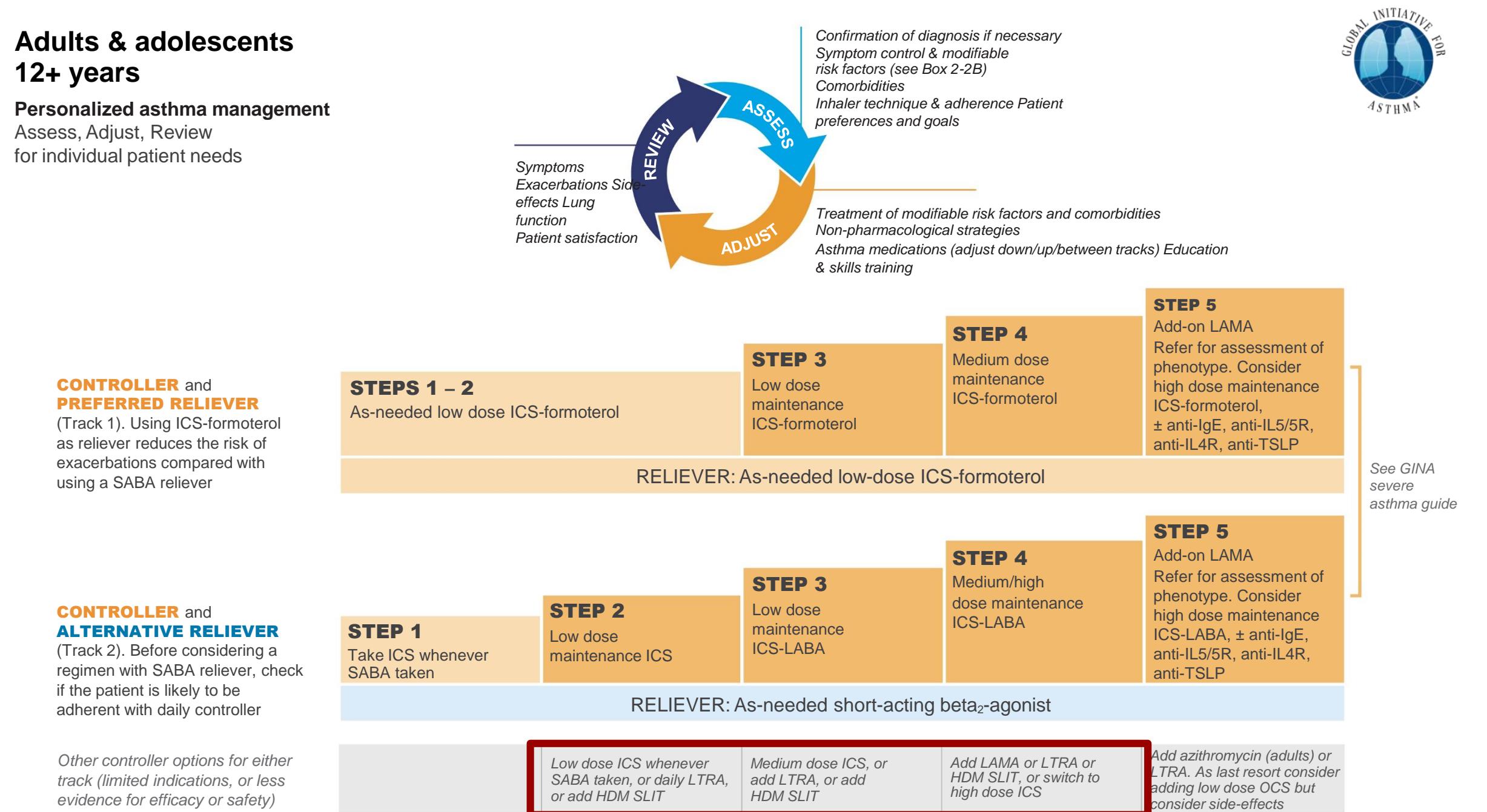
Personalized asthma management

Assess, Adjust, Review
for individual patient needs



CONTROLLER and
PREFERRED RELIEVER
(Track 1). Using ICS-formoterol
as reliever reduces the risk of
exacerbations compared with
using a SABA reliever

CONTROLLER and
ALTERNATIVE RELIEVER
(Track 2). Before considering a
regimen with SABA reliever, check
if the patient is likely to be
adherent with daily controller



Other controller options for either track (limited indications, or less evidence for efficacy or safety)

EAACI Guidelines on Allergen Immunotherapy: House dust mite-driven allergic asthma

1. Diagnose (symptoms, lung function, AHR, biomarkers, etc.)

- Atopic status (skin prick test, serum specific IgE)
- Component-resolved diagnosis
- Co-morbidities: atopic dermatitis, food allergy, AR

2. Characterise the allergic phenotype

History ± HDM provocation test

3. Evaluate the impact of allergic sensitisation on asthma symptoms and control

Asthma with HDM sensitisation

HDM-driven allergic asthma

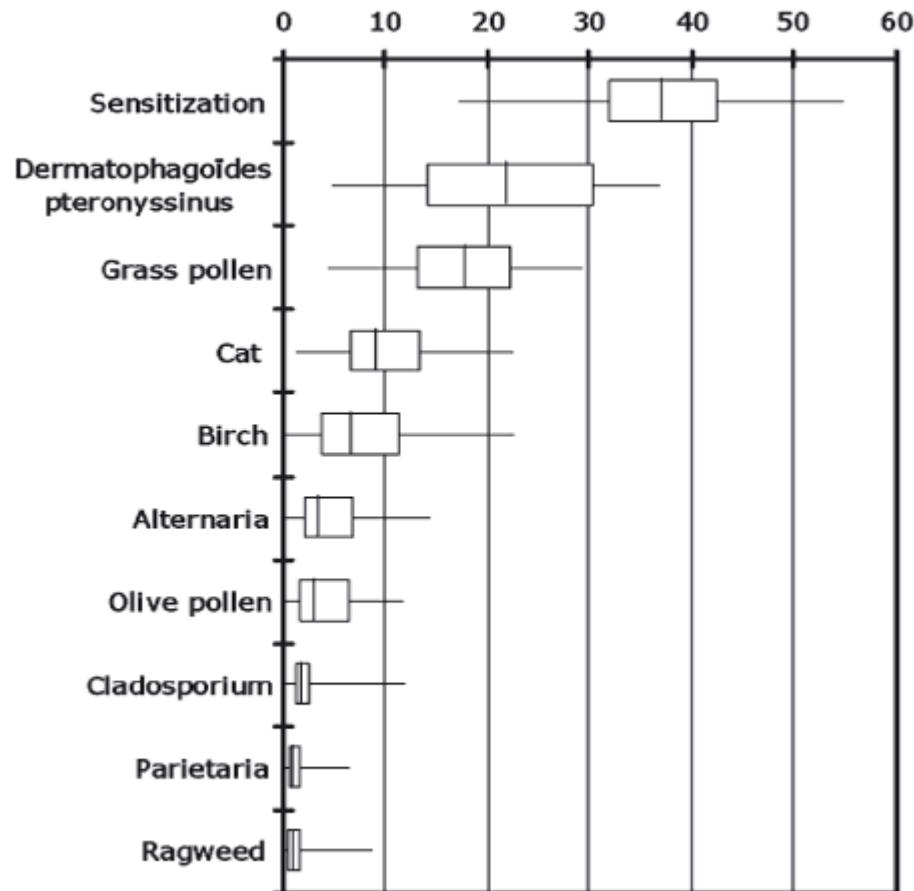
Regular controller treatment

Consider HDM AIT added to regular controller treatment



ECRHS: Sensitisation to aeroallergens

Bousquet et al. Allergy 2007



**n=18102, 22-44 y
35 Zentren, 15 Länder**

≥ 1 Allergen:	37%
<i>D. pteronyssinus:</i>	22%
Graspollen:	17%
Katzen:	9%

Hausstaubmilbenallergie

Heuschnupfen



Bewusstsein von Allergie

Perenniale Rhinitis/
Asthma



fehlendes Bewusstsein von Allergie

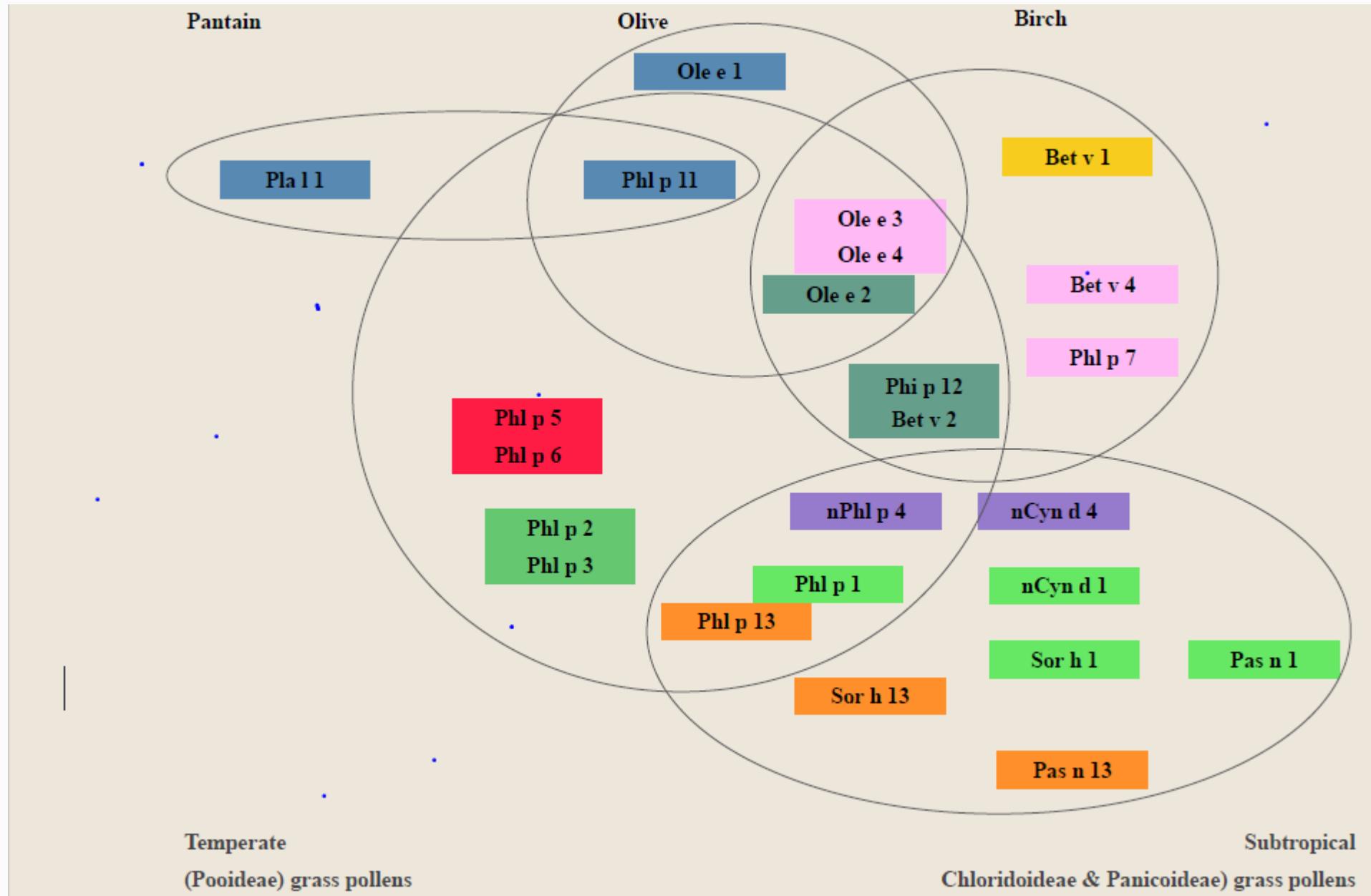
Kotbällchen mit Allergenen aus dem GIT der HSM (10-40µm)
trocknen, zerfallen (5-10µm) im Schwebestaub (aufwirbeln)



Ganzjährige Exposition geringer Allergenmenge
Chronische Entzündung der Nasenschleimhaut und Bronchien



Hauptbeschwerden nicht direkt allergenabhängig
ausgelöst durch Irritantien/unspezifische Reize
wie Anstrengung, Kälte, Abgase



Beifuss
Art v 1



Gräser
Phl p 1/5



Birke
Bet v 1



Oelbaum
Ole e 1



Art v 1 +
Phl p 7/12 +/-

Phl p 1/5 +
Phl p 7/12 +/-

Ole e 1 +
Phl p 7/12 +/-

Bet v 1 +
Phl p 7/12 +/-

Art v 1 -

Phl p 1/5 -

Ole e 1 -

Bet v 1 -



Hausstaubmilbenallergene

Table 2

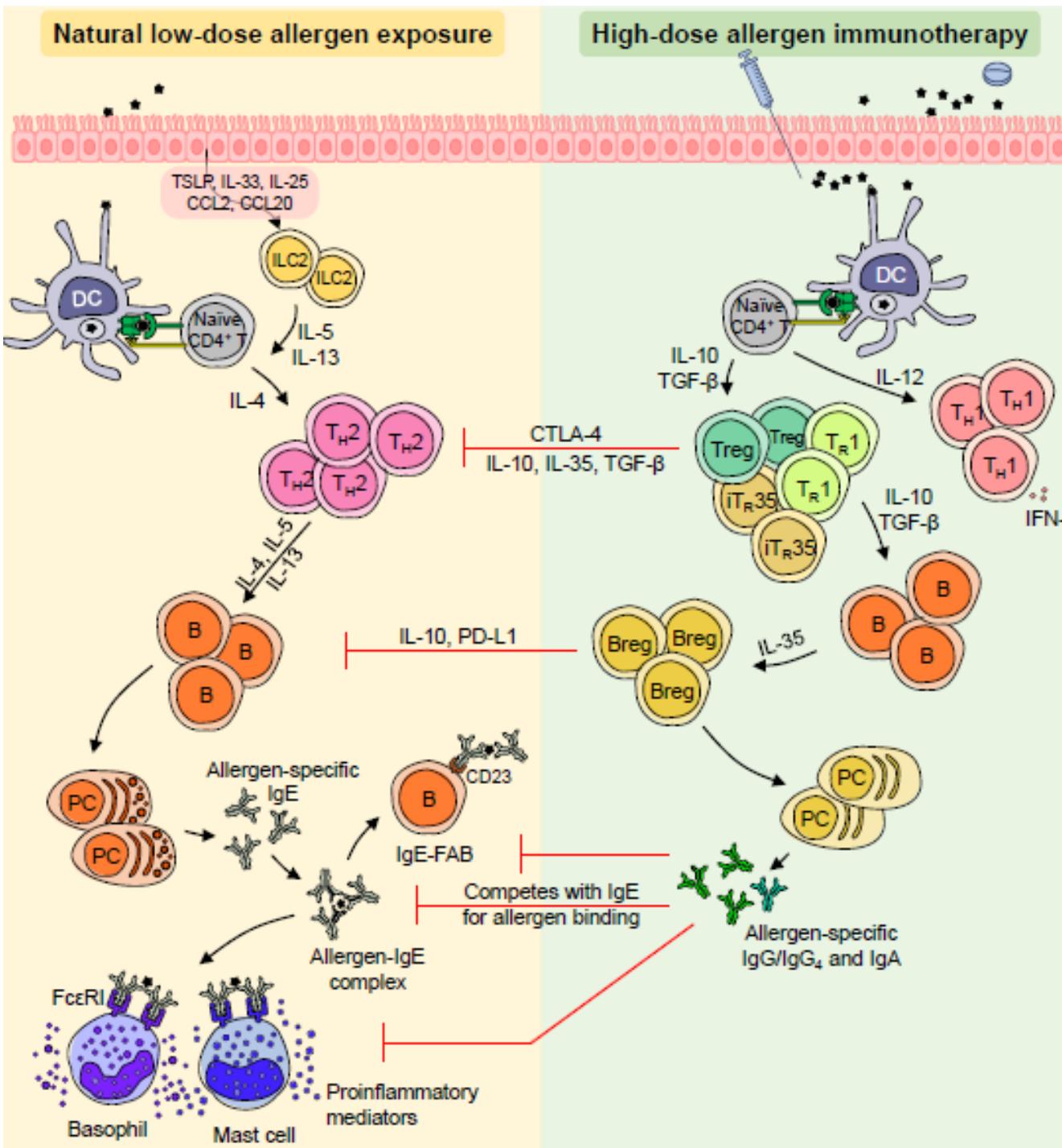
Main HDM allergen groups, taken from WHO-IUIS Database (www.allergen.org)

Allergen group	Biological function	<i>D. pteronyssinus</i>	<i>D. farinae</i>
1	Cysteine protease	24*	10
2	MD-2-like lipid binding protein	15	17
3	Trypsin-like serine protease	1	1
4	Amylase	1	1
5	Lipid binding protein	2	1
6	Chymotrypsin-like serine protease	1	1
7	Lipid binding protein	1	1
8	Glutathione-S-Transferase	1	1
9	Collagenase-like serine protease	2	
10	Tropomyosin	1	1
11	Paramyosin	1	1
12	Peritrophin		
13	Fatty acid binding protein	1	1
15	Chitinase	1	1
18	Chitinase	1	1
21	Lipid binding protein	1	1
23	Peritrophin-like protein	1	1
31	Cofilin	1	1
32	Pyrophosphatase	1	1
33	α -tubulin	1	1
35	MD2-like lipid binding protein		1

*Number of isoforms

**>20 Allergene
identifiziert und
charakterisiert:**

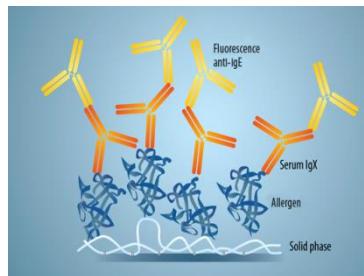
Klinisch relevant
Der p 1
Der p 2
Der p 5
Der p 7
Der p 21
Der p 23



Diagnostik der Milbenallergie



Pricktestung mit HSM-Extrakt (D. pteronyssinus, D. farinae)



sIgE in vitro (ImmunoCAP)

- Extrakt
- Der p 1/f 1, Der p 2/f 2 nur bei SIT



Provokationstestung

Allergen Immuntherapie in der CH: Produkte für SCIT



	Grass pollen	Children	Birch pollen	Children	Dust Mites	Children	Pets (cat & dog)	Children	Weed pollen	Children	Bee & wasp venom	Children
Pre- seasonal	Allergovit®	>5	Allergovit®	>5	-	-	-		Allergovit®	>5	-	
	Polvac®	>6	Polvac®	>6	-	-	-	-	-	-	-	
Perennial	Alutard®	>5	Alutard®	>5	Alutard®	>5	Alutard®	>5			Alutard®	>5
	-	-	-		Novo Helisen®	>5	-	-	-	-	-	

* Admitted and available in Switzerland (October 2020)



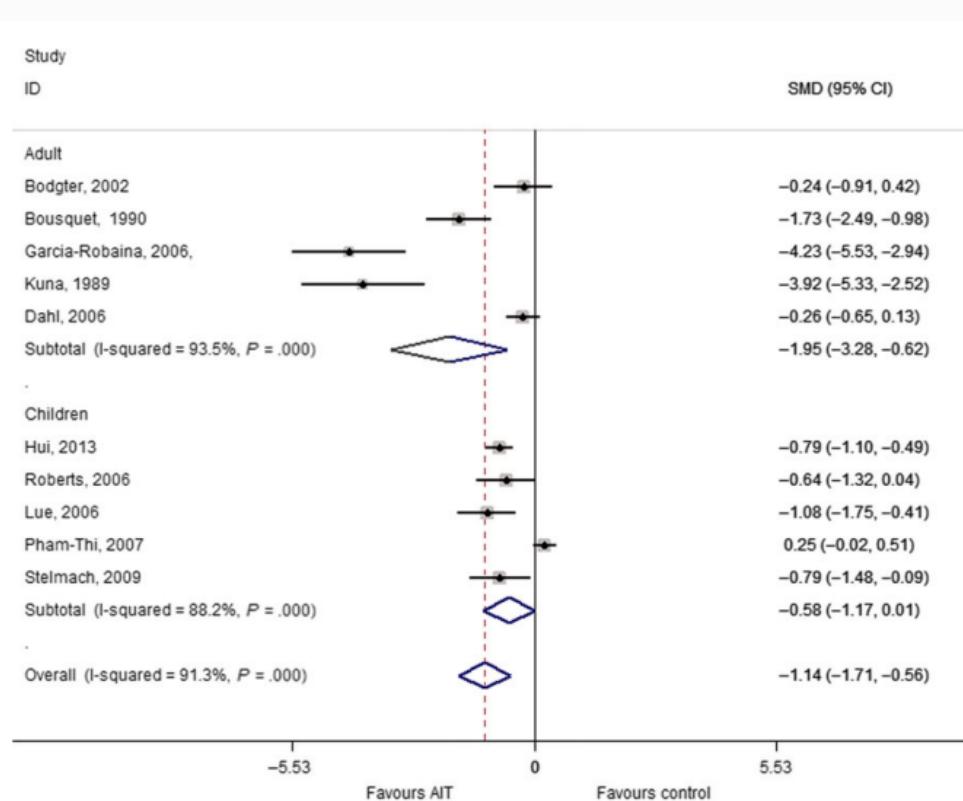
Allergen Immunotherapy in the CH: Products for SLIT

	Grass pollen	Children	Birch pollen	Children	Dust Mites	Children	Pets (cat & dog)	Children	Weed pollen	Children	Bee & wasp venom	Children
Pre- & co-seasonal or perennial	Grazax®	>5	Itulazax®	>12	Acarizax®	>12	-	-	-	-	-	-
	Oralair®	>5	Staloral®	>5	-	-	-	-	-	-	-	-

* Admitted and available in Switzerland (October 2020)



Allergen immunotherapy for allergic asthma: A systematic review and meta-analysis



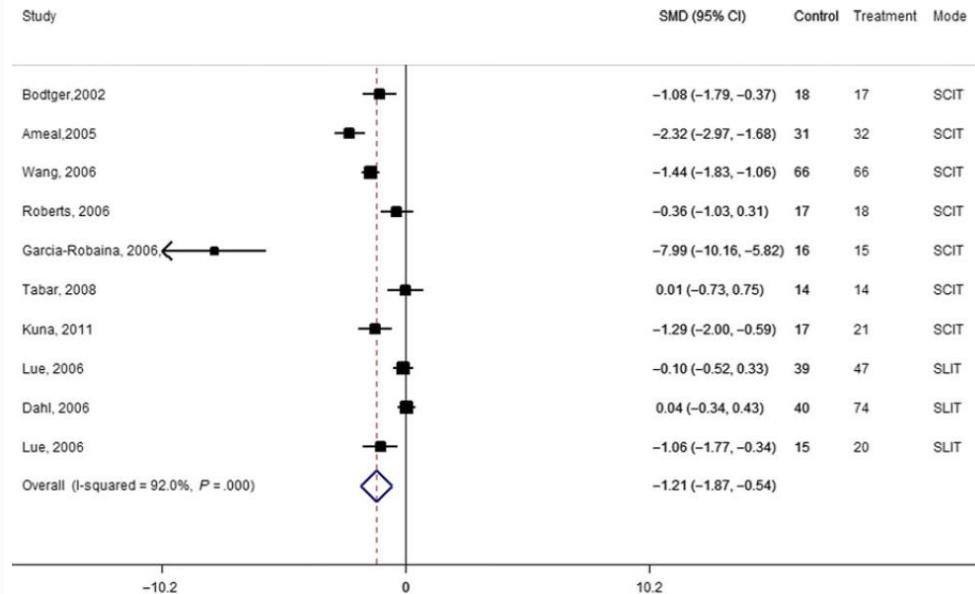
Symptomen-Score (short-term)

- **Nach Abschluss AIT (SCIT und SLIT): starker Effekt der AIT**
- **In Kindern und Erwachsenen**
- **SCIT etwas besser als SLIT**
- **v.a. bei mild/moderatem Asthma**
- **Für HSM, Graspollen: starker Effekt**
- **Für Katzen und Hundeallergene: mässiger Effekt**

Meta-analysis of doubleblind RCTs, comparing symptom scores between AIT (SLIT and SCIT) and placebo, groups in children <18 vs adults ≥18 y (random-effects model)

Dahmi et al Allergy 2017

Allergen immunotherapy for allergic asthma: A systematic review and meta-analysis



Meta-analysis of doubleblind RCTs, comparing medication Scores between AIT (SLIT and SCIT) and placebo groups (random-effects model)

Medikation-Score (short term)

- Nach Abschluss AIT (SCIT und SLIT): grosser Effekt der AIT
- In Kindern besser als in Erwachsenen

Dahmi et al Allergy 2017

Which patients with asthma are most likely to benefit from allergen immunotherapy?

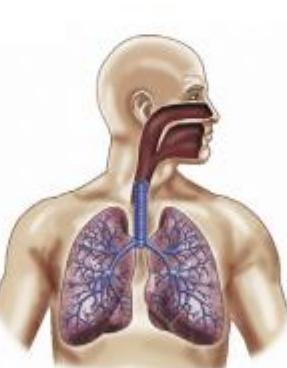
WHO WOULD BE A GOOD CANDIDATE FOR SUCCESSFUL ALLERGEN IMMUNOTHERAPY FOR ASTHMA?



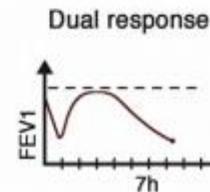
High Eosinophils



Inhaled corticosteroid



Rhinitis



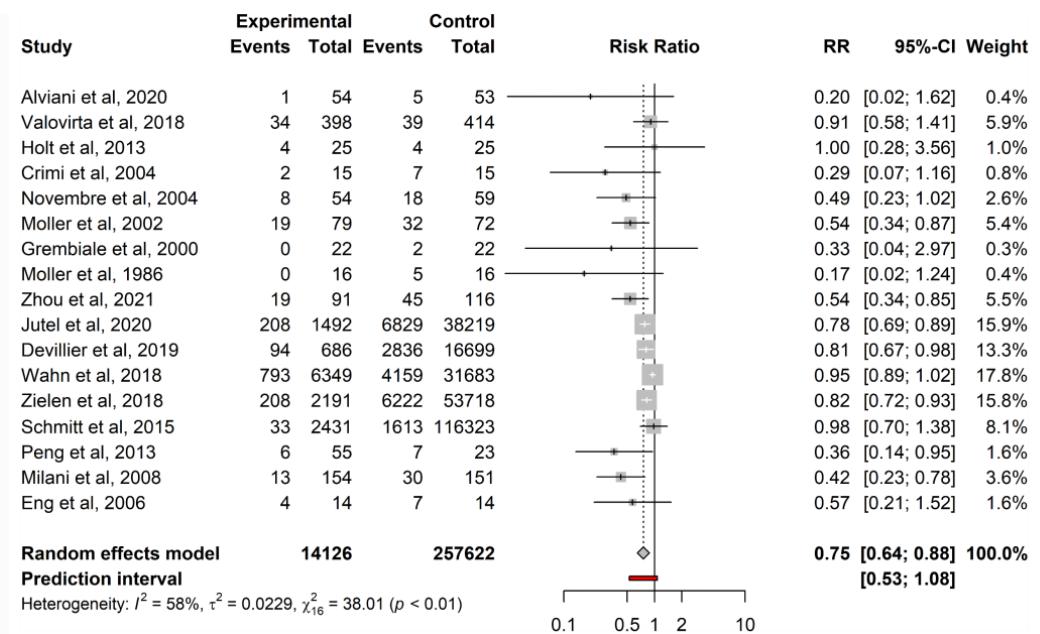
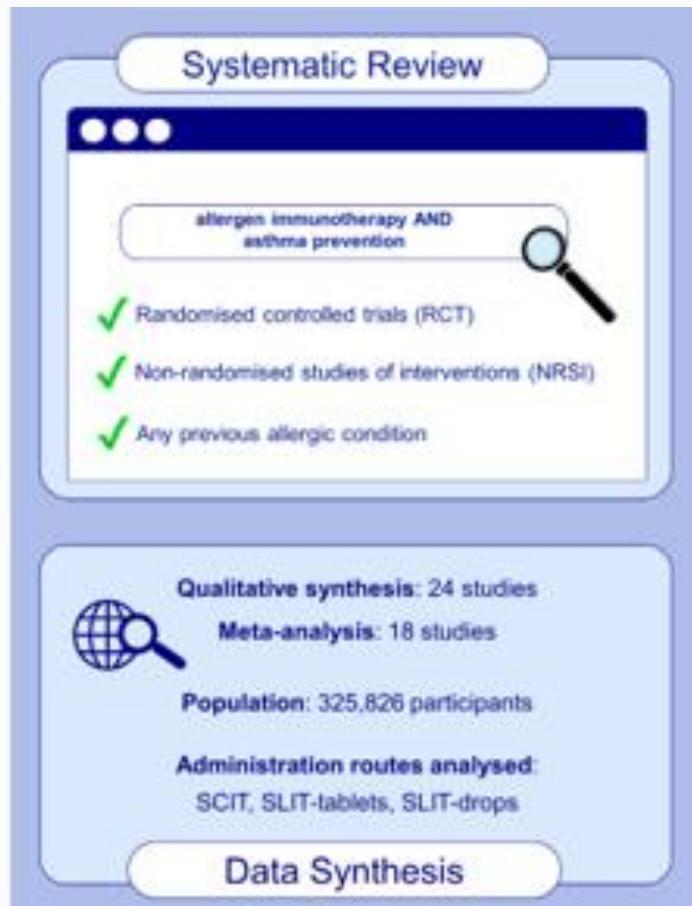
SCIT signifikanten Effekt auf asthmatische Sofortreaktion gegen HSM, Graspollen, Birkenpollen, Katzen, bei Kindern und Erwachsenen

HDM SLIT Tabletten wirksam bezüglich Asthma Exazerbationen und ICS Reduktion als Add-on-Therapie bei Erwachsenen

Polysensibilisierte Patienten mit Rhinitis und GINA 2-4 Asthma profitieren am meisten

Biological zur Verbesserung von LUFU und Asthma Kontrolle vor AIT?

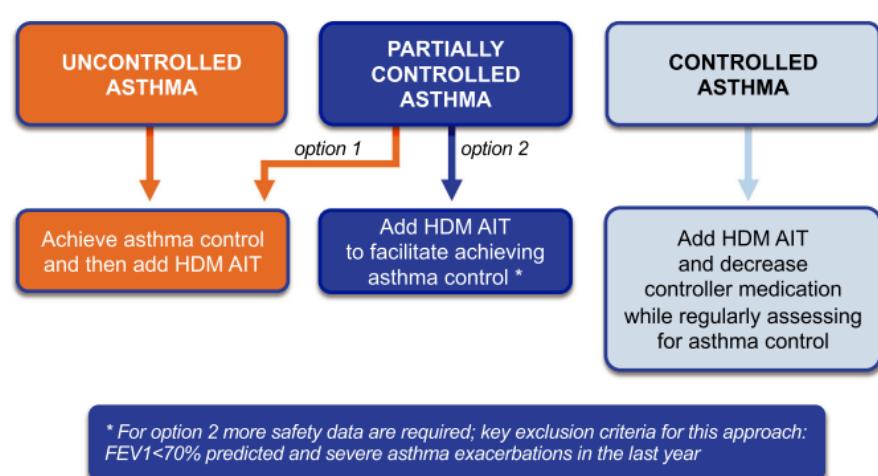
Allergen immunotherapy for asthma prevention: A systematic review and meta-analysis of randomized and non-randomized controlled studies



AIT senkt das Risiko ein Asthma bronchiale zu entwickeln um 25%

- unabhängig ob SCIT oder SLIT
- unabhängig ob Graspollen oder HDM

EAACI Guidelines on Allergen Immunotherapy: House dust mite-driven allergic asthma



1. Asthma Kontrolle und LUFU regelmässig erfassen
2. Patienten mit partiell kontrolliertem Asthma oder mit Anamnese von schweren Asthma Exazerbationen während der letzten 12 Monate regelmässig monitorisieren
3. Wenn keine Wirksamkeit nach einem Jahr, ev AIT sistieren

Unkontrolliertes Asthma

= wichtigster unabhängiger Risikofaktor für schwere und fatale Nebenwirkungen
= wichtigste Kontraindikation für HDM SCIT und SLIT

Patienten mit schwerem aber kontrolliertem HDM driven Asthma in Ausnahmefällen mit sehr engmaschigem Monitoring

EAACI Guidelines on Allergen Immunotherapy: House dust mite-driven allergic asthma

TABLE 6 Contraindications and precautions for HDM AIT in patients with HDM-driven allergic asthma

	Remarks	Key reference
HDM AIT is contraindicated in uncontrolled asthma	Due to safety concerns.	Epstein 2016, ⁹⁰ Calderon 2017, ⁹¹ Rodríguez del Rio 2017, ⁹² Normansell 2015, ⁵⁹ Pitsios 2015, ⁹³ Cox 2011, ⁹⁴ Lockey 2001, ⁹⁵ Bernstein 2004 ⁹⁶
HDM SLIT-tablet may be considered with caution in partially controlled asthma	HDM AIT might be beneficial especially in patients with partly controlled HDM-driven allergic asthma with studies demonstrating improved asthma control and quality of life. HDM SLIT-tablet in adults with asthma not well controlled by ICS or combination products did not increase the risk of major adverse events (AEs) ⁶⁵ ; however, FEV ₁ less than 70% of predicted value or severe asthma exacerbation within 3 months before randomization were key exclusion criteria.	Mosbech 2014 ⁶⁵ Virchow 2016 ⁶⁷
AIT should not be initiated in pregnancy (but can be continued in pregnancy)	Safety of initiation and continuation of SCIT and SLIT during pregnancy analyzed in 4 studies totaling 422 women demonstrated increased incidence of prematurity, hypertension/proteinuria, congenital malformations or perinatal deaths during pregnancy, and no fetal complications following systemic AEs while receiving AIT ⁹⁴	Pitsios 2015 ⁹³ Oykhman 2015 ⁹⁷
AIT should not be initiated in patients with active or uncontrolled autoimmune disorders (AID)	The CONSID survey reported on patients undergoing AIT with AID. Major problems were infrequent ⁷⁸	Pitsios 2015 ⁹³ Rodríguez del Rio 2017 ⁹²
AIT should not be initiated in patients with active malignancies		Pitsios 2015 ⁹³
AIT may be considered with caution in patients with controlled asthma under treatment with beta-blockers (BB) or ACE inhibitors (ACEI)	Only in specialized settings due to increased refractoriness to treatment of anaphylaxis with epinephrine. The CONSID survey reported on patients undergoing AIT under BB or ACEI. Major problems were infrequent ⁷⁸	Rodríguez del Rio 2017 ⁹²
AIT is not recommended in patients with immune deficiencies, active infections, and infestations and uncontrolled diseases such as diabetes, inflammatory bowel disease, gastric ulcer, etc.	The CONSID survey reported on patients with immune deficiencies or under immune suppressants receiving AIT. Major problems were infrequent ⁷⁸	Pitsios 2015 ⁹³ Rodríguez del Rio 2017 ⁹²

HSM AIT kontraindiziert bei unkontrolliertem Asthma
HDM SLIT kann mit Vorsicht bei partiell kontrolliertem Asthma erwogen werden

Weitere Kontraindikationen:

- Schwangerschaft (Beginn)
- aktive und nicht kontrollierte Autoimmunerkrankung
- “aktive” maligne Erkrankung
- Immundefizienz
- aktive Infektionen,
- unkontrollierte Erkrankungen wie Diabetes, IBD, Magenulzera
- ACE-Hemmer/Betablocker (relative)

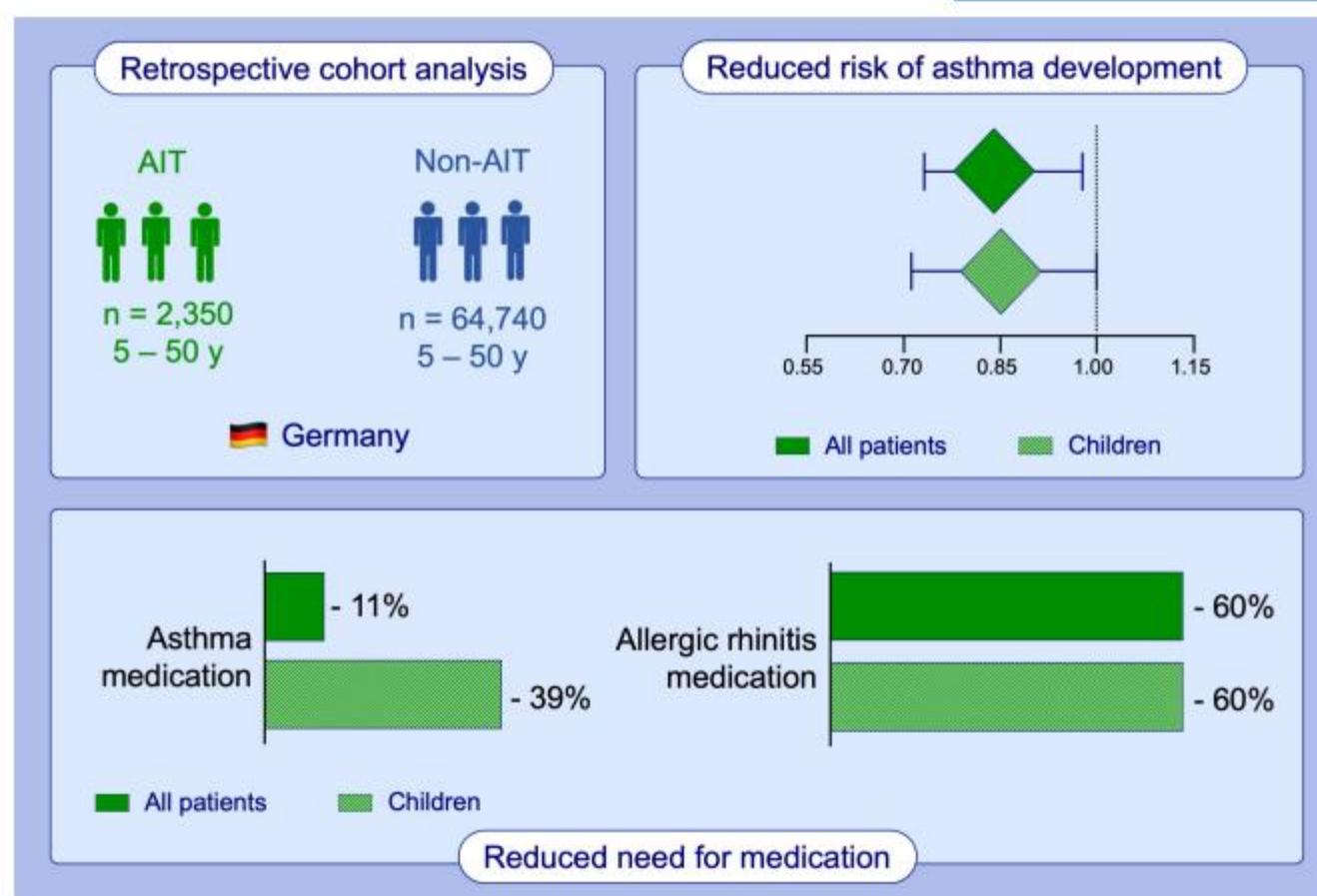
Nicht erwähnt aber klare KI SLIT: Eosinophile Oesophagitis

EAACI Guidelines on Allergen Immunotherapy: House dust mite-driven allergic asthma

TABLE 7 Recommendations for risk management of HDM AIT in HDM-driven allergic asthma

HDM SCIT for HDM-driven allergic asthma	<ul style="list-style-type: none">• Signed informed consent• Supervised administration by a healthcare professional (HCP) trained in the evaluation of patients with allergic conditions in a setting facilitating proper management of systemic reactions• Assessment of the patient's current health status before the administration of SCIT to determine whether there have been any recent changes in the patient's health that may require modifying or withholding treatment (eg, uncontrolled/symptomatic asthma or exacerbation of allergy symptoms)• Observation for at least 30 minutes after injection• Patient education for management and reporting late reactions
Home based HDM SLIT for HDM-driven allergic asthma	<ul style="list-style-type: none">• Signed informed consent• Supervised initiation by a HCP trained in the evaluation of patients with allergic conditions in a setting facilitating proper management of systemic reactions• Observation for at least 30 minutes after the first dose• Patient education and written instructions on how to recognize and manage adverse reactions and when to contact the HCP for adverse reactions, treatment gaps, or other events that may affect treatment (eg, new medication or illness), how to manage missed doses and the situations when they should withhold SLIT• In cases of oral inflammation, such as mouth ulcers, lichen planus, stomatitis aphthous, or dental extractions, administration of SLIT should be temporarily discontinued until there is complete healing of the oral cavity. Dental flossing and gum hygiene can be associated with gum bleeding. It is recommended that the patient delay the administration of SLIT for a few hours after cessation of gum bleeding. It is suggested to resume SLIT 24 hours after a dental cleaning procedure.• Recommendations for when to withhold SLIT dose to avoid potential situations when systemic allergic reactions may be more likely should also be provided.• Regular follow-up care with a HCP trained in the evaluation of patients with allergic conditions to monitor safety.

Real-world evidence of subcutaneous allergoid immunotherapy in house dust mite-induced allergic rhinitis and asthma



2350 Patienten mit Milben-Allergoid-SIT
64740 Kontrollpatienten

- Signifikant weniger Asthma Entwicklung
- Signifikant weniger Asthma/Rhinitis Medikation

Allergen Immuntherapie: Sicherheit SCIT

Overall

- **Large local reactions**
 - Pruritus and/or erythema (> 2.5 cm) on injections site
 - 26-86% of patients
- **Systemic reactions**
 - 1.08% of patients or 0.01% of injections
- **Lethal reactions**
 - 1 every 2.5 million injections
 - Risk factors: >75% uncontrolled asthma, wrong dosage, inadequate administration of epinephrine, prior history of systemic reactions (4x higher!)

Children

- **Local reactions**
 - Pruritus and/or erythema (> 2.5 cm) on injections site
 - up to 54% of SCIT
- **Systemic reactions including respiratory reactions such as**
 - mild to severe bronchospasm in 1% to 30% of patients or up to 4.6% of injections
 - urticaria in 2% to 19% of patients
- **No reports of anaphylaxis or death**

James and Bernstein. Allergen Immunotherapy: An Updated Review of Safety. *Curr. Opin. Allergy Clin. Immunol.* 2017; 17, 55–59.
Allergen-Specific Immunotherapy for Pediatric Asthma and Rhinoconjunctivitis: A Systematic Review. *PEDIATRICS* Volume 131, Number 6, June 2013

Allergen Immuntherapie: Sicherheit SLIT

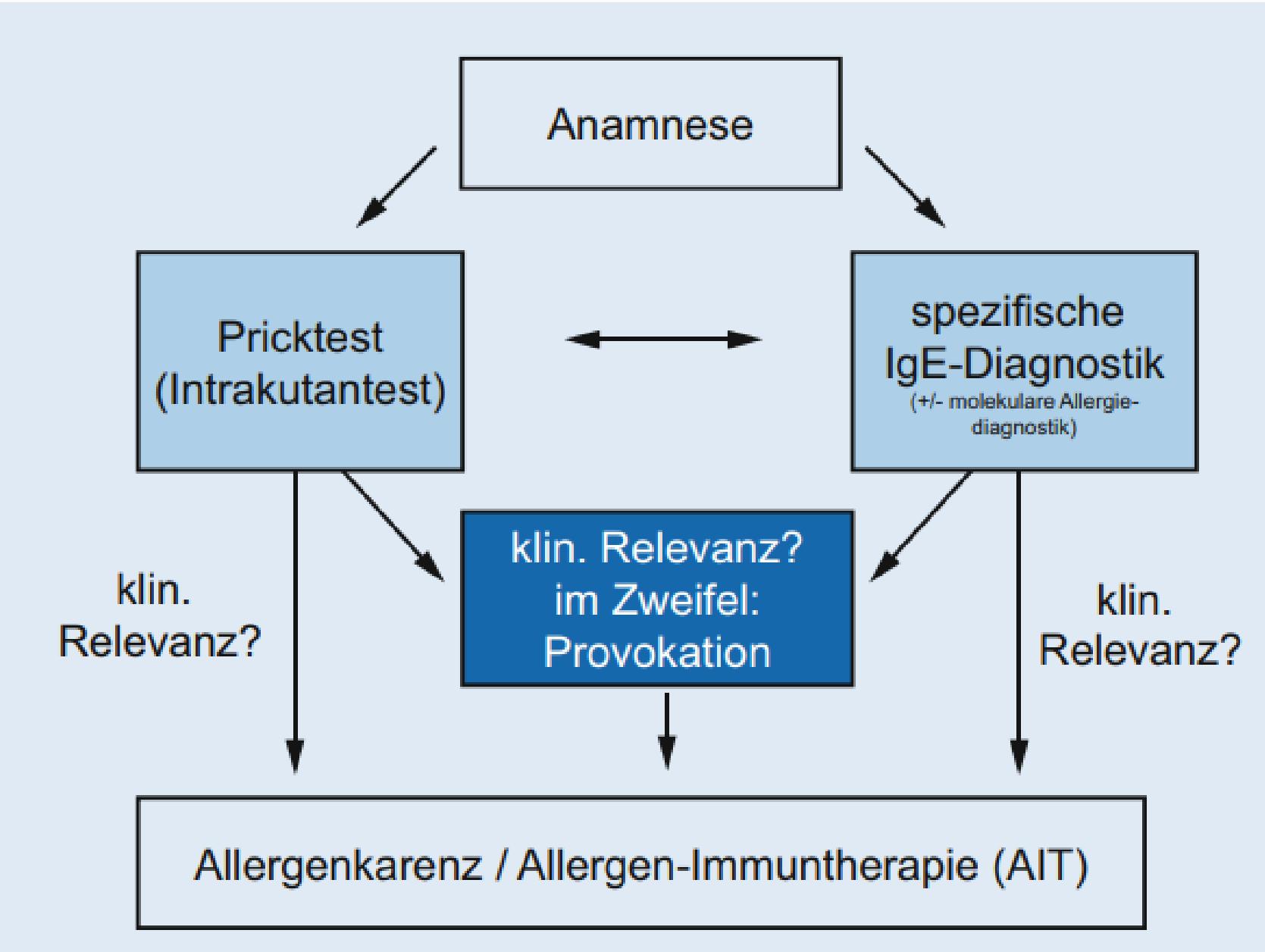
Overall

- Local reactions
 - Oro-mucosal and gastrointestinal symptoms
 - About 79% of patients
 - Usually transient and self-resolving symptoms
- Systemic reactions
 - 2.7 reactions every 1000 SLIT doses
 - Only 0.056% classified as severe (abdominal pain, vomit, urticaria)
 - Risk factor:
 - uncontrolled asthma (about 1/3)

Children

- Local reactions
 - Oro-mucosal and gastrointestinal symptoms
 - 0.2% to 50% of patients
- Systemic reactions are rare
- No life-threatening reactions, anaphylaxis, or deaths

James and Bernstein. Allergen Immunotherapy: An Updated Review of Safety. Curr. Opin. Allergy Clin. Immunol. 2017; 17, 55–59.
Allergen-Specific Immunotherapy for Pediatric Asthma and Rhinoconjunctivitis: A Systematic Review. PEDIATRICS Volume 131, Number 6, June 2013



Efficacy +++
Safety +

SCIT

Efficacy ++
Safety ++

SLIT



Patient in equipoise