

Allergy vaccines: the importance of the active principle

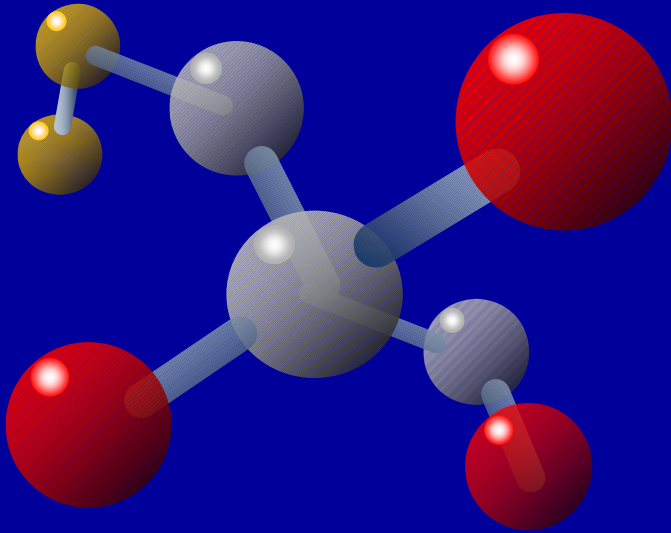
more important than the pharmaceutical form,
either tablets, drops or injections!

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2010

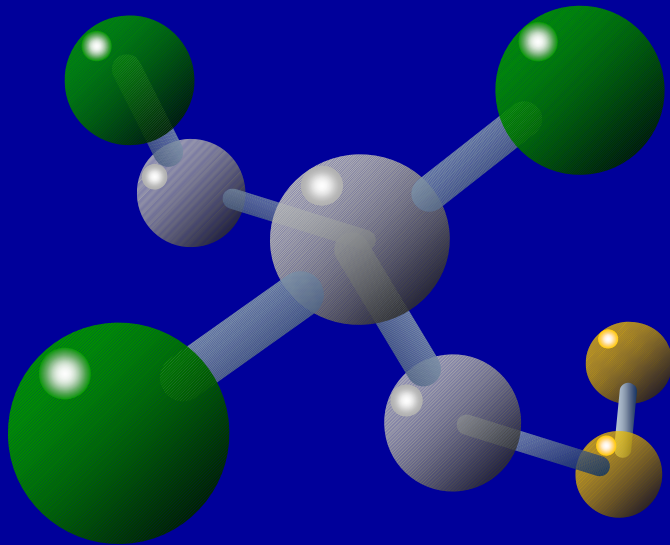
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The Allergen



This is a simplification of an **allergen** molecule, for example of a weed.

The Carbamylated Allergoid



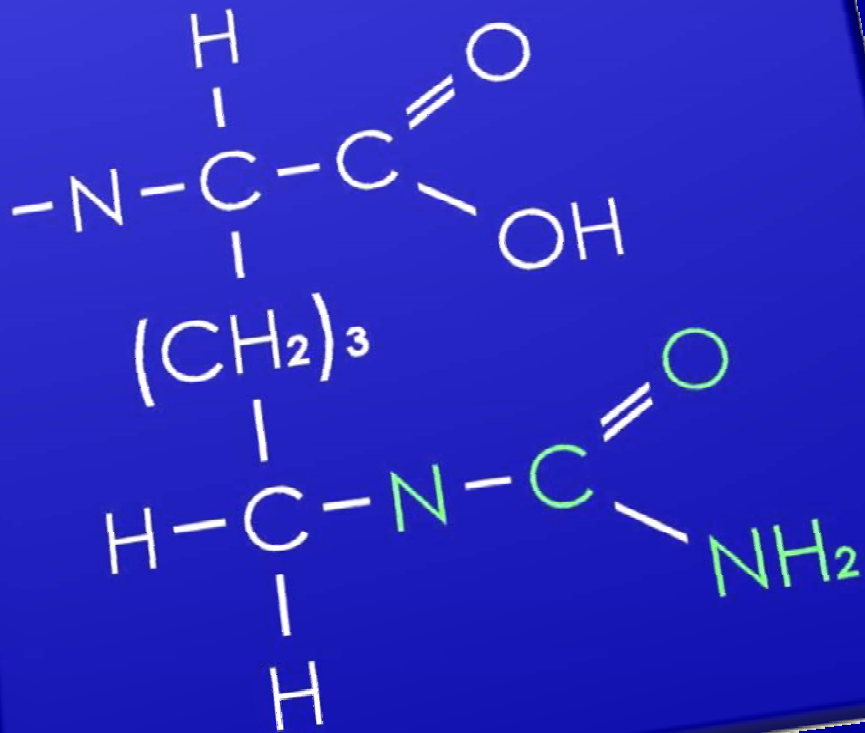
This is a simplification of an **allergoid** molecule, a chemical modification of an **allergen**.

The Carbamylated Allergoid is obtained by carbamylation with potassium cyanate at alkaline pH, a reaction that leads to a substantial substitution of the allergen lysine aminogroups: a **well-definite** active principle.

(Mistrello et al, Allergy 1996)

what are the consequences ?

Carbamylated Allergoid



1

Dramatic reduction
of specific IgE linking

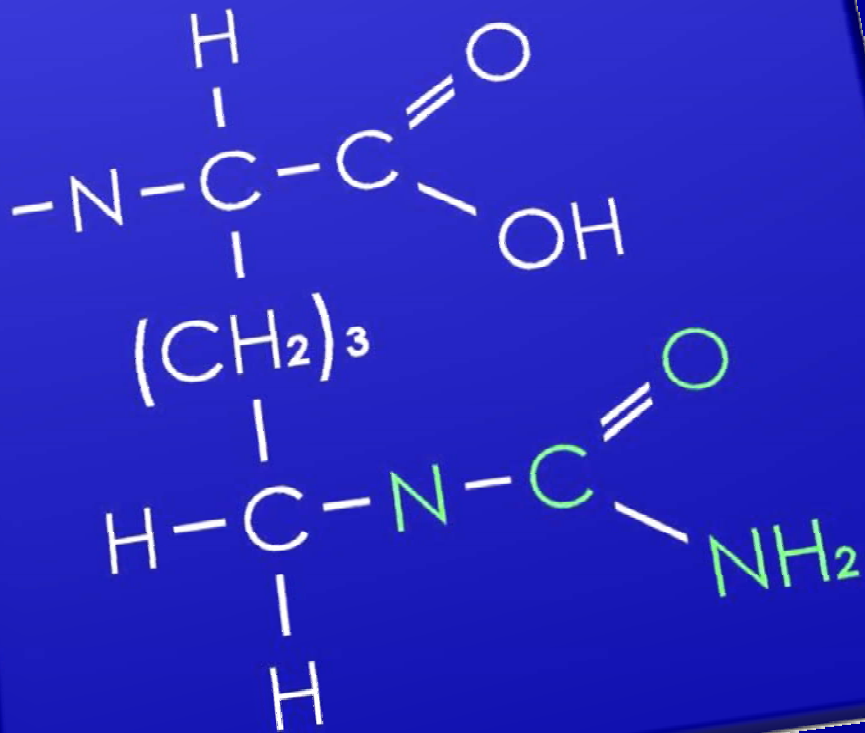
reduced
allergenic activity



SAFETY

what are the consequences ?

Carbamylated Allergoid



2

Resistance to enzymatic degradation

carbamylated allergoid
remains active

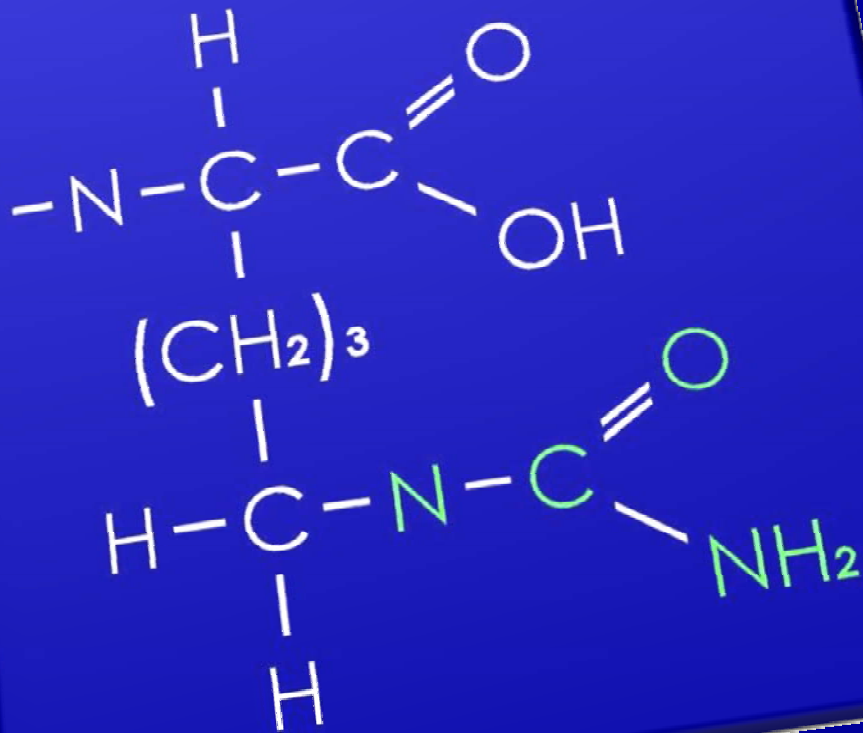


"high doses" are not necessary.

EFFECTIVE DOSES

what are the consequences ?

Carbamylated Allergoid



3

NO
alteration of T-epitopes

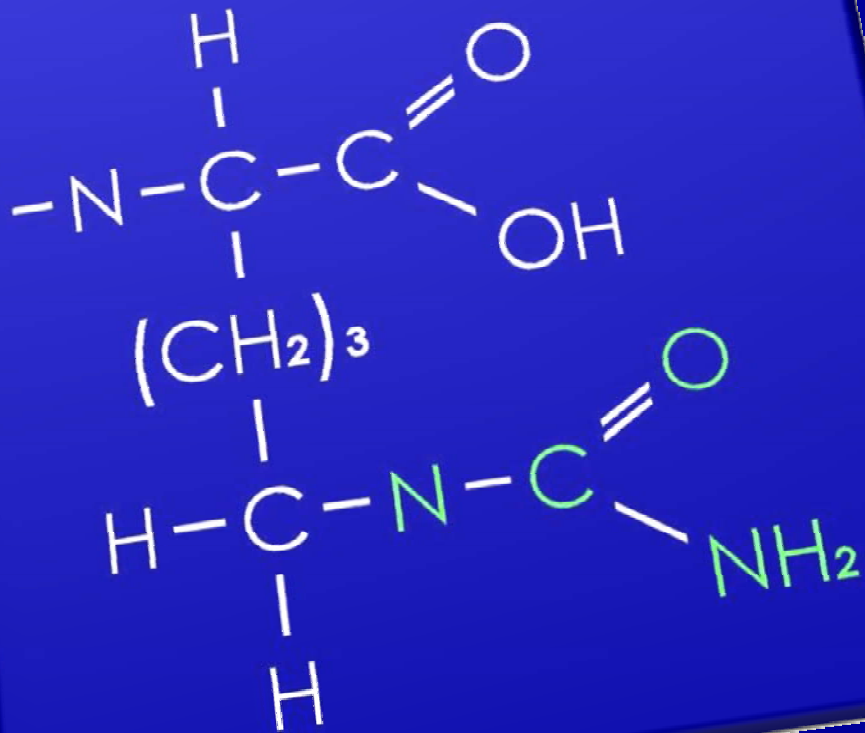
preserved
immunogenic activity



EFFICACY

what are the consequences ?

Carbamylated Allergoid



4

PRESERVATION
of molecular sizes

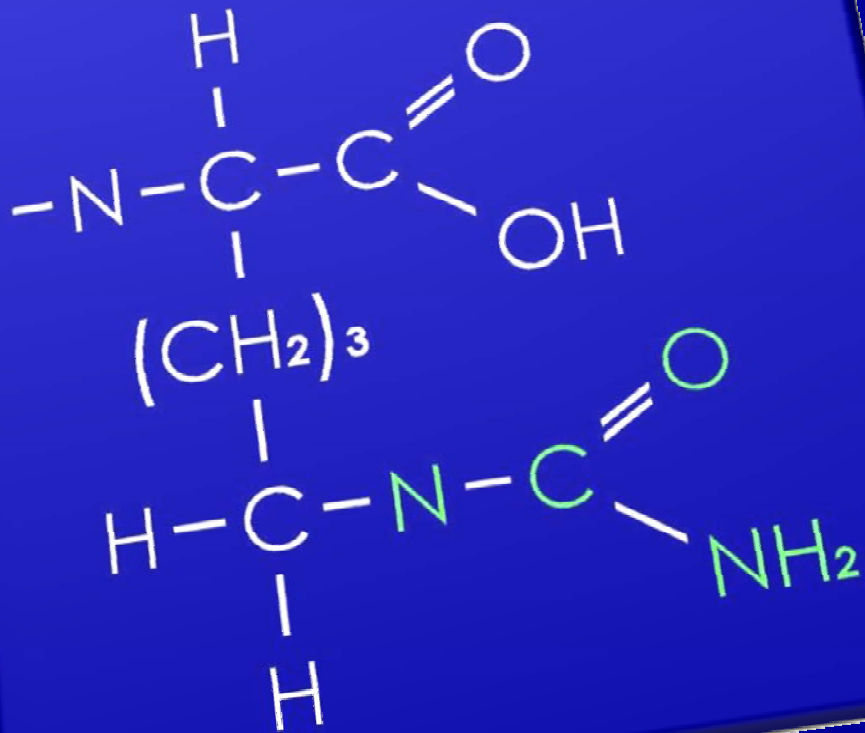
Carbamylated Allergoid is
a Monomeric Allergoid



FIT for SLIT

what are the consequences ?

Carbamylated Allergoid



5

IRREVERSIBILITY
of carbamylation

NO back to
native allergen



SAFETY

selected references

Synopsis of published Lais studies

Part 1: study design

AUTHOR	JOURNAL	Study	Adults/ Children	No. Patients	Diseases*	Allergen	Treatment	Tablets/Drops
Bordignon	Giom II Allergol Immunol Clin 1994;4:153-159	DBPC	adults, children	60	OR and/or A	Grass	preseasonal	Tab
Pacor	Rec Prog Med 1996;87(1):4-6	open	adults	34	OR	Grass	preseasonal	Tab
Caffarelli	Allergy 2000;55:1142-7	DBPC	children	48 (24A+24P)	R, C or A	Grass	preseasonal	Tab
Lombardi	J Invest Allergol Clin Immunol 2001;11:41-45	open	adults	51 (26A+25C)	RC and/or A	Grass	preseasonal	Tab
Palma-Carlos	Allergol Immunopathol 2006;34(5):194-198	DBPC	adults	33	R with or without A	Grass	preseasonal	Tab
Burastero	Ann All Ast Imm 2006;100:343-350	open	adults	11	R	Grass	preseasonal	Tab
Pacor	Rec Prog Med 1995;86(12):489-91	open	adults	14	A	Mites	continuous	Tab
La Rosa	Not Allergol 1996;15:45-46	open	children	30	A and/or RC	Mites	continuous	Tab
Passalacqua	The Lancet 1996;351:629-32	DBPC	adults	20 (10A+10P)	RC	Mites	continuous	Tab
Marogna	Int Journ Imm Pharm 2001;14:93-101	observational (SLIT, SIT, intranasal)	adults	29 A + 12 C (SLIT)	OR with or without A	Mites	continuous	Tab
Passalacqua	Allergy 2006;61:849-854	DBPC	adults	56 (A+ P)	R	Mites	continuous	Tab
Cosmi	Clin Exp All 2006;36:261-292	open	adults	25 (A+C)	R with or without A	Mites	continuous	Tab
Ippoliti	Pediatr Allergy Immunol 2006;17:337-345	open	children	40	A	Mites	continuous	Drops
Marogna	Int Arc All Imm 2007;142:70-78	retrospective	adults	65 (53 A+12C)	R	Mites	continuous	Tab
Marogna	Eur Ann Allergy Clin Immunol 2008;40:22-29	retrospective	adults	101 (57 A+44C)	R	Mites	continuous	Tab
Ariano	Invest Allergol Clin Immunol 1996;8(3):155-160	DBPC	adults	30 (15A+15P)	R with or without A	Parietaria	pre-co-seasonal	Tab
D'Anneo	Allergol Immunopathol 2006;36(2):79-84	open	adults	65 (24A+21A+21C)	R and/or A	Parietaria	coseasonal	Tab
Lombardi	Allergy 2001;56:989-992	open (safety)	adults	198	R and/or A	Mites(50), Grass(75), Olive(1), birch(4), Parietaria(45)	preseasonal or continuous	Tab
Marogna	Eur Ann All Imm Clin 2003;35(4):133-140	observational (SLIT, SIT, intranasal)	adults, children	106 A (Lais)+ 170 C	R and A	Mites(44), Grass(98), birch(32), Parietaria(45)	continuous	Tab
Rossi	Giom II Allergol Immunol Clin 2002;12:221-228	open (safety)	adults	13	R and/or A	Grass + Mites	-	Tab
Arena	Int Journ Imm Pharm 2003;16:277-282	open	adults	60	R with or without A	Mites(29), Grass(5), Olive(2), Parietaria(24)	preseasonal or continuous	Tab
Agostinis	Allergy 2005;60:133	open (safety)	children	36	A or R	Mites, Grass	continuous	Drops
Gammeri	Allergol Immunopathol 2005;33(3):142-4	open (safety)	adults, children	105 (28 o+77a)	R or A	Mites(56), Grass(15), Parietaria(34)	-	Tab
Rossi	Int J Immunopathol Pharmacol 2005;16:277-285	open (safety)	adults	45	RC and/or A	Grass + Mites	-	Tab
Giordano	Eur Ann All Imm Clin 2006;38(9):310-312	open	adults	39	R with or without A	Mites(27), Grass(7), Olive(3), Cat(1), Parietaria(1)	continuous	Tab
La Grutta	Eur Ann Clin Immunol 2007;39:40-44	open	adults/ children	56 (33A+ 23C)	A with or without R	Mites + Parietaria	continuous	Tab
Burastero	Int J Immunopathol Pharmacol 2009;22:343-352	open	adults	11	R	Birch	pre-co-seasonal	Tab
Mezei	Not Allergol 1996;15:40-44	DBPC	adults/ children	60 (30A+30C) 20A+10P in each group	RC with or without A	Ragweed	pre-co-seasonal	Tab
Ariano	Eur Ann All Imm Clin 2005;37(3):103-108	open	adults	30 (20A+10C)	RC and/or A	Cypress	pre-co-seasonal	Drops
Rolla	EAACI 2009	open	adults	21	RC and/or A	Birch	pre-co-seasonal	Tab

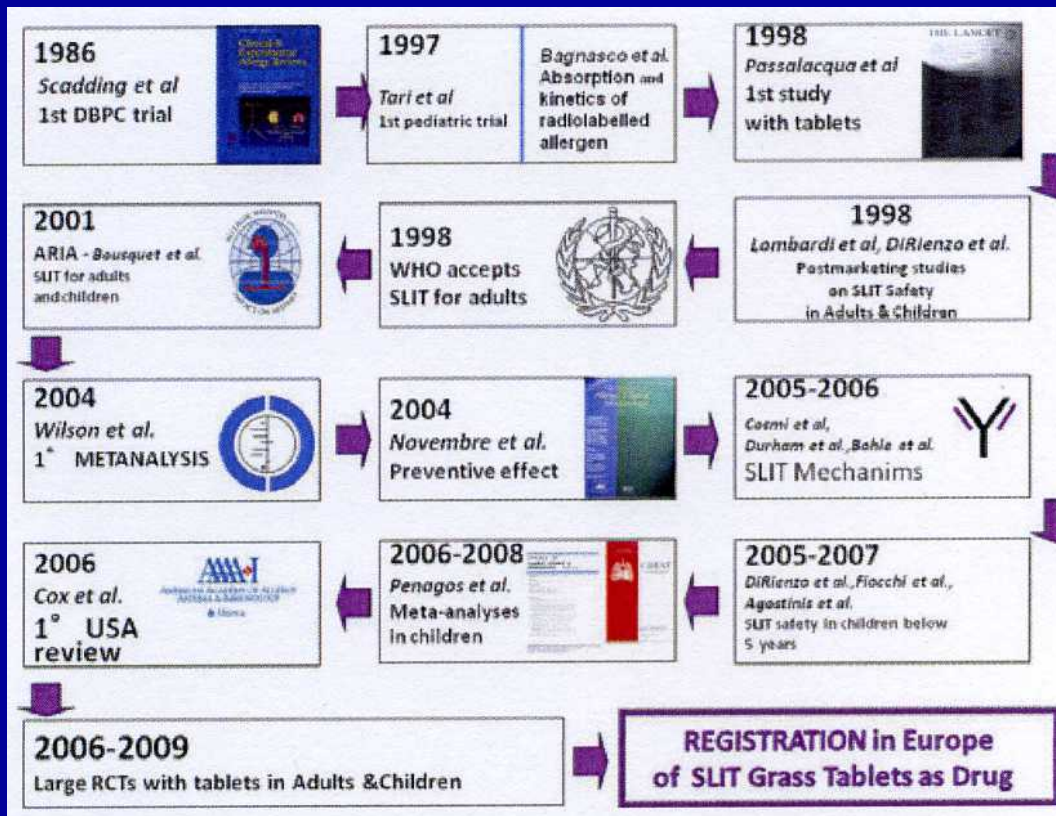
OR = Oculo-Rhinis; A = Asthma; C = Conjunctivitis; RC = Rhino-Conjunctivitis

Synopsis of published Lais studies

Part 2: results

AUTHOR	JOURNAL	Treatment		Results Symptoms	Results Drugs	Results Mch	Cumulative dosages in AU/year
		Build up	Maintenance AU				
Bordignon	Giom II Allergol Immunol Clin 1994;4:153-159	14 weeks	1000/week	reduction	reduction	-	36,500
Pacor	Rec Prog Med 1996;87(1):4-6	14 weeks	1000/week	reduction	reduction	-	36,500
Caffarelli	Allergy 2000;55:1142-7	7 weeks	3000/week	reduction	=	-	37,250
Lombardi	J Invest Allergol Clin Immunol 2001;11:41-45	14 weeks		reduction	reduction	reduction bronch. reac.	36,000
Palma-Carlos	Allergol Immunopathol 2006;34(5):194-198	14 weeks	2000/week	reduction	reduction	reduction nasal reac.	40,500
Burastero	Ann All Ast Imm 2006;100:343-350	-	14000/week	-	-	-	120,000
Pacor	Rec Prog Med 1995;86(12):489-91	14 weeks	1000/week	reduction	-	reduction	62,500
La Rosa	Not Allergol 1996;15:45-46	3 weeks	300/week	reduction	reduction	-	23,775
Passalacqua	The Lancet 1996;351:629-32	14 weeks	4000/week	reduction	reduction	reduction CMM, ECP	176,500
Marogna	Int Journ Imm Pharm 2001;14:93-101	14 weeks	2000/week	reduction	reduction	reduction bronch. reac.	100,000
Passalacqua	Allergy 2006;61:849-854	4 weeks	2000/week	reduction	reduction	quality of life improvement	116,000
Cosmi	Clin Exp All 2006;36:261-292	8 weeks	1000/week	reduction	-	immunological eval. (L-10)	60,000
Ippoliti	Pediatr Allergy Immunol 2006;17:337-345	4 weeks	1800/week	reduction	-	reduction bronch. reac.	43,950
Marogna	Int Arc All Imm 2007;142:70-78	14 weeks	1000/week	reduction	-	reduction bronch. reac.	62,500 (1 year) 218,500 (4 years)
Marogna	Eur Ann Allergy Clin Immunol 2008;40:22-29	14 weeks	1000/week	reduction	-	reduction bronch. reac.	62,500
Ariano	Invest Allergol Clin Immunol 1996;8(3):155-160	14 weeks	2000/week	reduction	reduction	reduction nasal reac.	72,525
D'Anneo	Allergol Immunopathol 2006;36(2):79-84	3 days	1000 or 3000/week	reduction (VAS)	reduction	reduction bronch. reac.	32,000 or 84,000
Lombardi	Allergy 2001;56:989-992	8 weeks	2000/week	-	-	-	20,850 or 104,800
Marogna	Eur Ann All Imm Clin 2003;35(4):133-140	14 weeks	1000/week	reduction	reduction	reduction bronch. reac.	62,500
Rossi	Giom II Allergol Immunol Clin 2002;12:221-228	2 hours	2000/week	-	-	-	-
Arena	Int J Immunopathol Pharmacol 2003;16:277-282	14 weeks	4000/week	reduction	reduction	-	176,500
Agostinis	Allergy 2005;60:133	3 weeks	4200/week	reduction	-	-	216,000
Gammeri	Allergol Immunopathol 2005;33(3):142-4	20 minutes	2000/week	-	-	-	-
Rossi	Int J Immunopathol Pharmacol 2005;16:277-285	20 minutes	2000/week	-	-	-	-
Giordano	Eur Ann All Imm Clin 2006;38(9):310-312	4 days	2000/week	reduction (VAS)	reduction	-	108,000
La Grutta	Eur Ann Clin Immunol 2007;39:40-44	16 days	2000/week	reduction	reduction	reduction bronch. reac.	110,000
Burastero	Int J Immunopathol Pharmacol 2009;22:343-352	-	15,000/month	reduction	reduction	immunological eval. (L-10)	90,000
Mezei	Not Allergol 1996;15:40-44	8 weeks	2000/5 week 1000/5 week	reduction	reduction	reduction nasal reac. signific. in ad.	33300
Ariano	Eur Ann All Imm Clin 2005;37(3):103-108	16 days	900/week	reduction	reduction	reduction nasal reac.	22,900
Rolla	EAACI 2009	-	6000/week or 2000/week	reduction	reduction	-	120,000 or 208,000
Fancello	EAACI 2008	4 days	1000/week	reduction (VAS)	-	-	57,000

The contribution of carbamylated allergoid in the history of SLIT

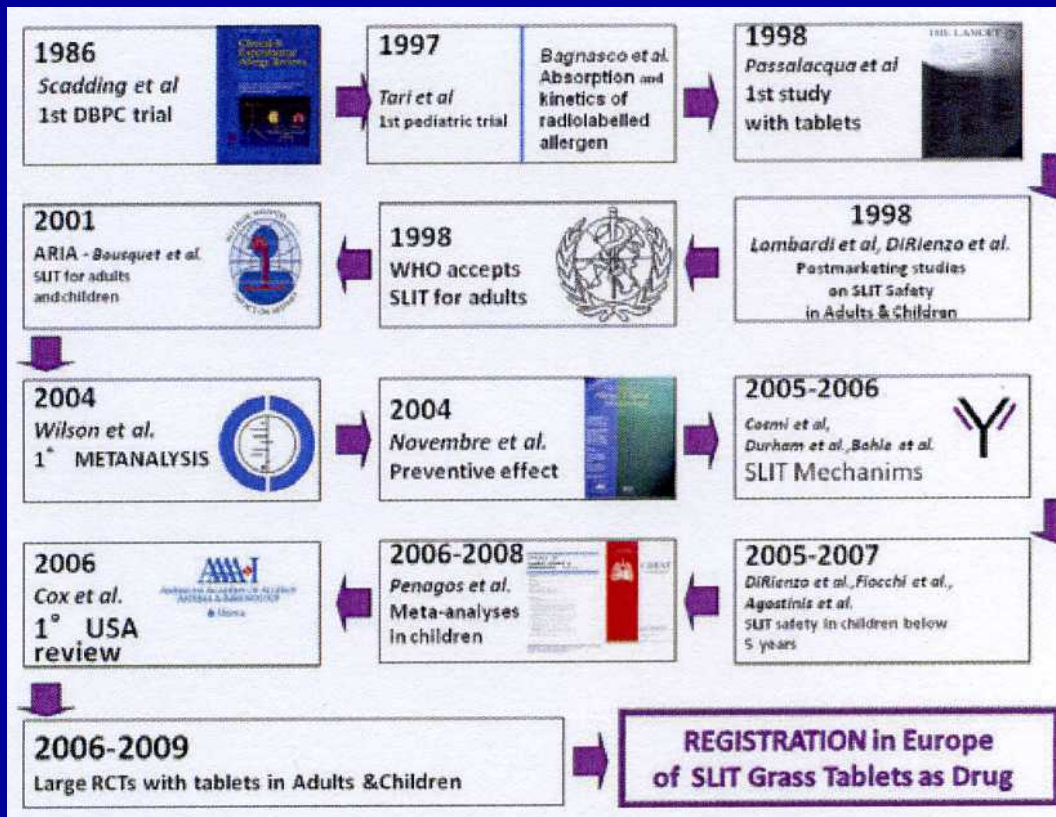


1997

Bagnasco, JACI

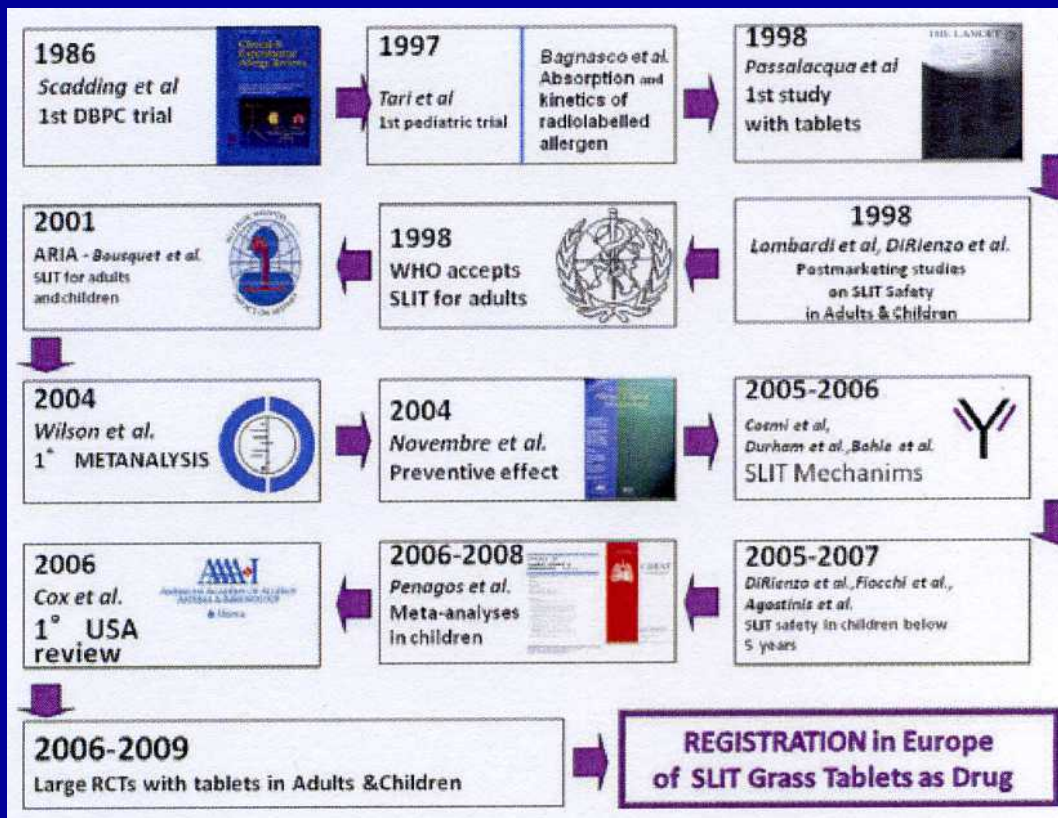
1^o study on kinetics

The contribution of carbamylated allergoid in the history of SLIT



1998
Passalacqua, Lancet
1^o study with
tablets,
allergoid tablets

The contribution of carbamylated allergoid in the history of SLIT

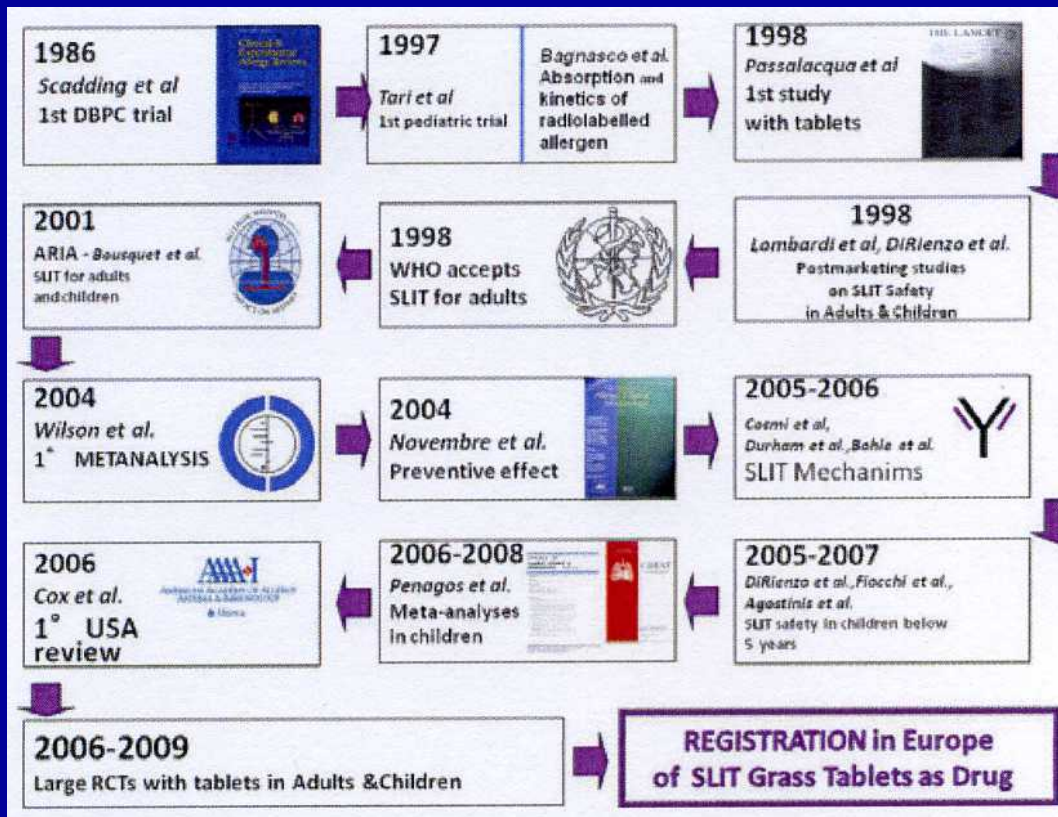


2000

Caffarelli, Allergy

1st study with
tablets
in children

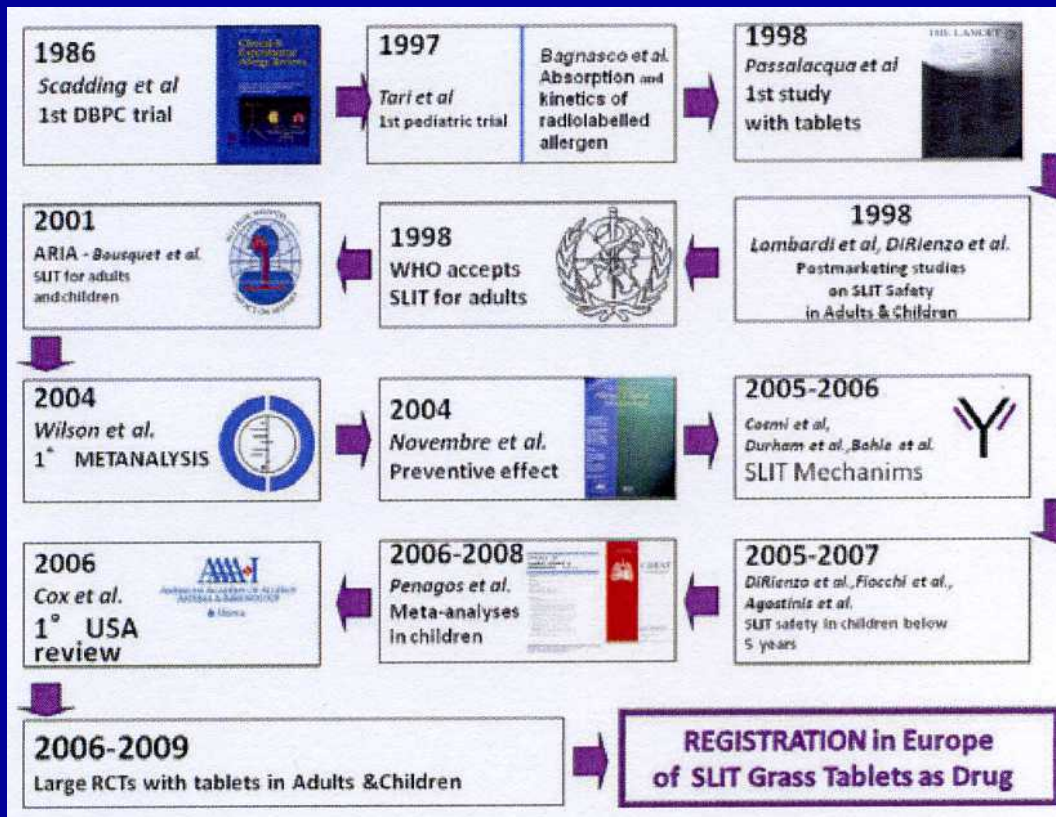
The contribution of carbamylated allergoid in the history of SLIT



2001
Bagnasco, Allergy

Comparison
between
allergoid tablets
VS
allergen in tablets
and in solution

The contribution of carbamylated allergoid in the history of SLIT

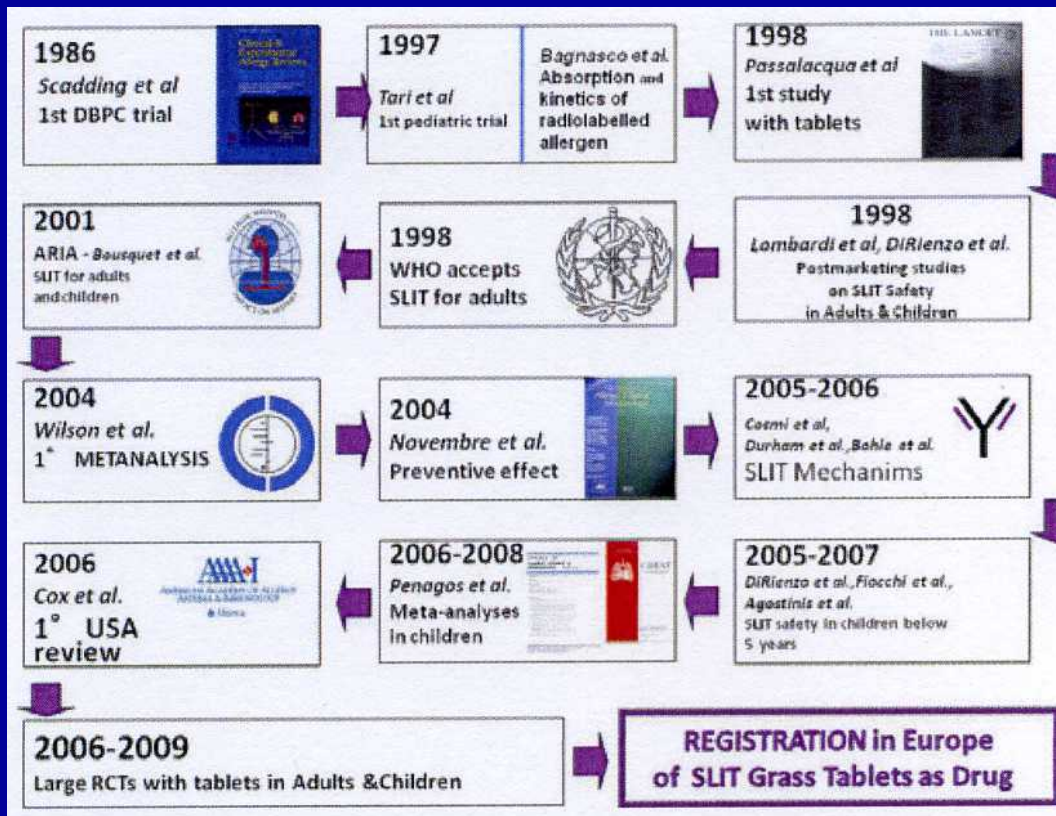


2004

Lombardi, JACI

Adherence
to allergoid SLIT

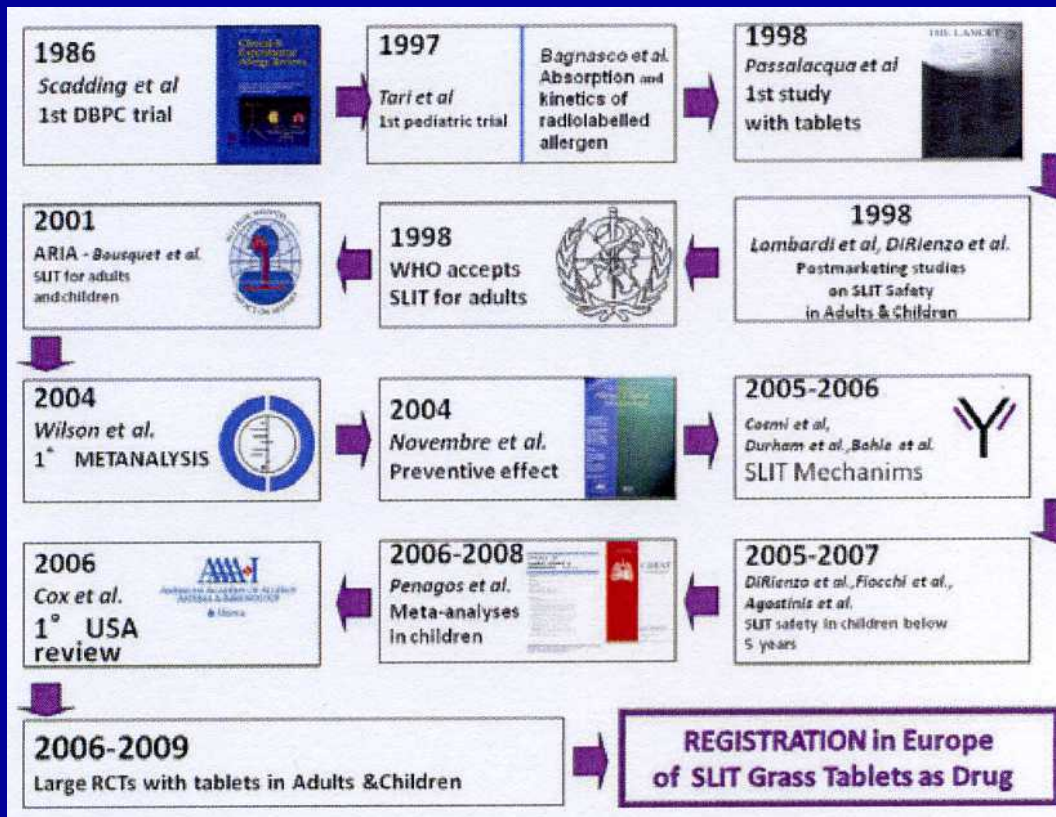
The contribution of carbamylated allergoid in the history of SLIT



2005
Agostinis, Allergy

Safety
in children

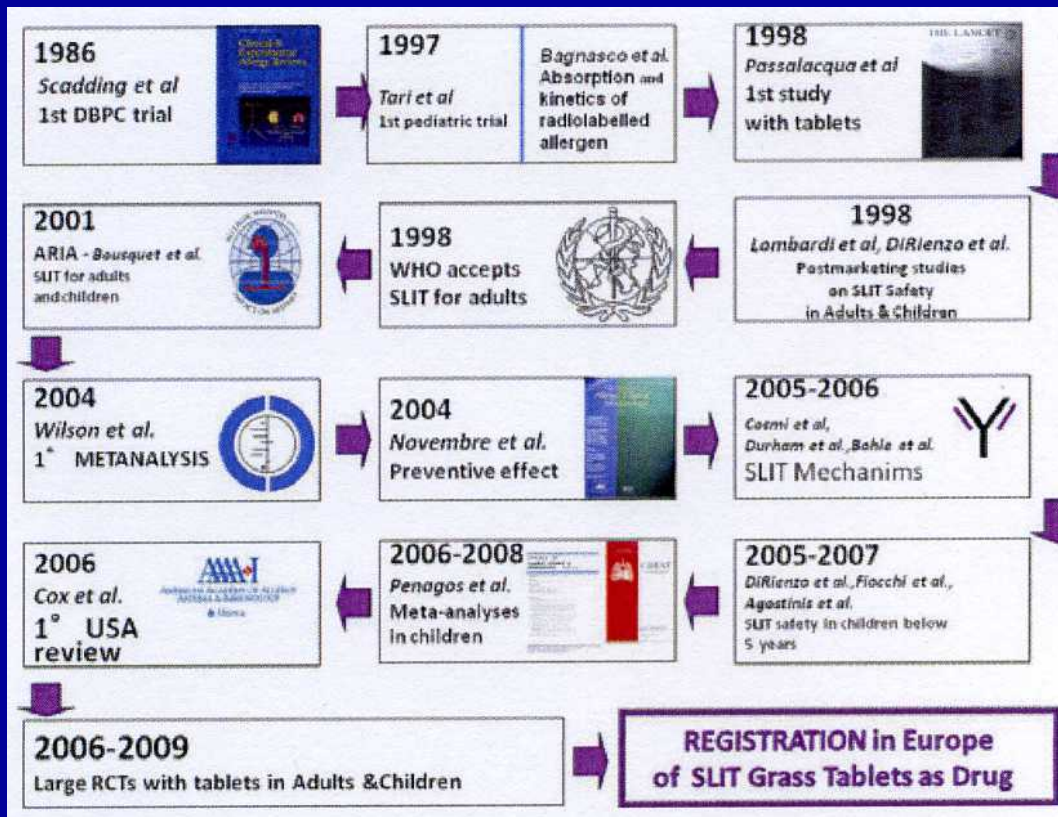
The contribution of carbamylated allergoid in the history of SLIT



2006
Cosmi, Clin Exp Allergy

Allergoid SLIT
mechanism

The contribution of carbamylated allergoid in the history of SLIT

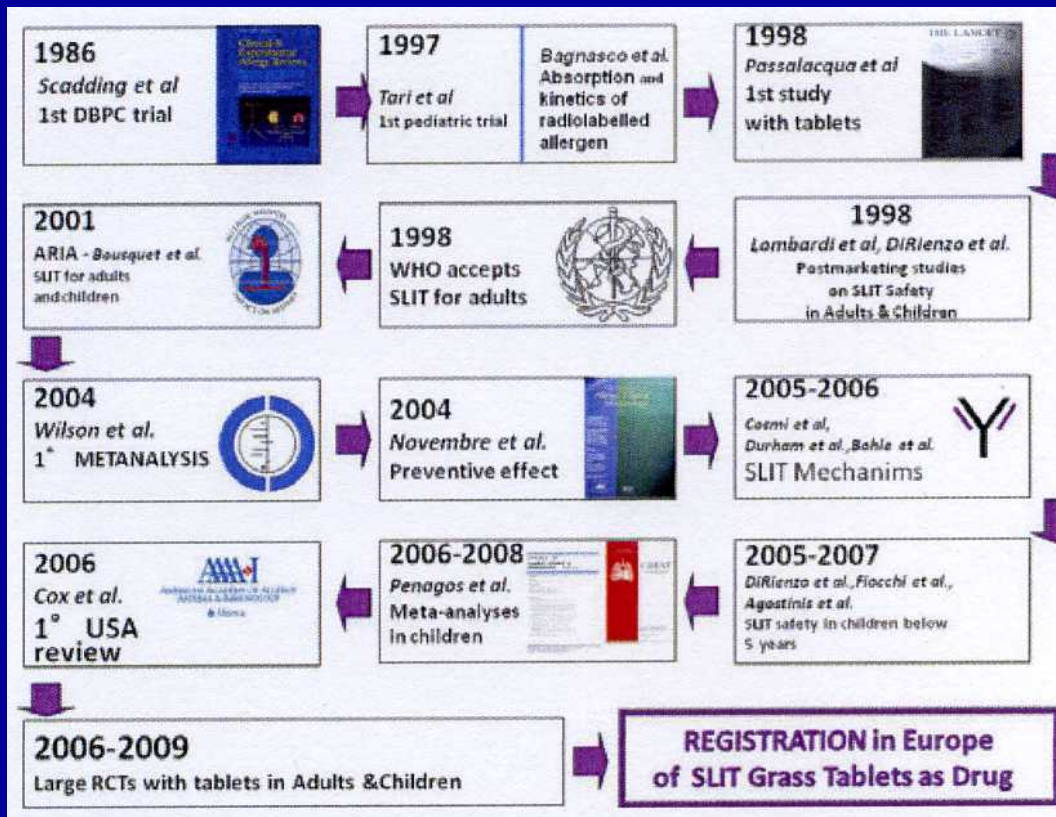


2009

D'Anneo, Int J Imm Pharm

Allergoid SLIT safety
and tolerability with
4-day
induction phase

The contribution of carbamylated allergoid in the history of SLIT



2010

Passali, Acta ORL

Allergoid SLIT safety
and tolerability
without
induction phase

A final snapshot on the market...

Allergen SLIT

Alk - Grazax
Alk - SLITOne
Alk - SLITOne plus
Allergopharma - Allerslit
Bencard - Oralvac
HAL – Sublivac
Novartis - Tol SL
Roxall - Sulgen spray
Stallergenes - Oralair
Stallergenes - Staloral
Themocare - Allerbio sublingual

Allergoid SLIT

Lofarma - Lais tablets
Lofarma - Lais drops