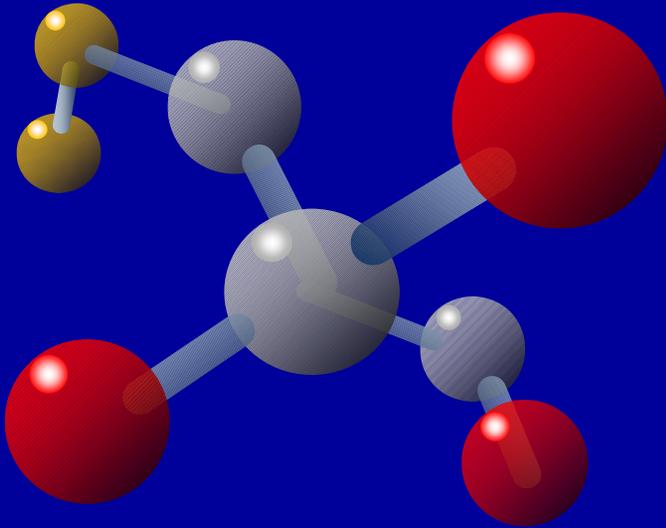


Противоаллергические вакцины:
Значение основного
действующего вещества
более важно, чем фармацевтическая форма, - будь то
таблетки, капли или инъекции!

Allergy vaccines:
the importance of the active principle
more important than the pharmaceutical form,
either tablets, drops or injections!

Аллерген

The Allergen



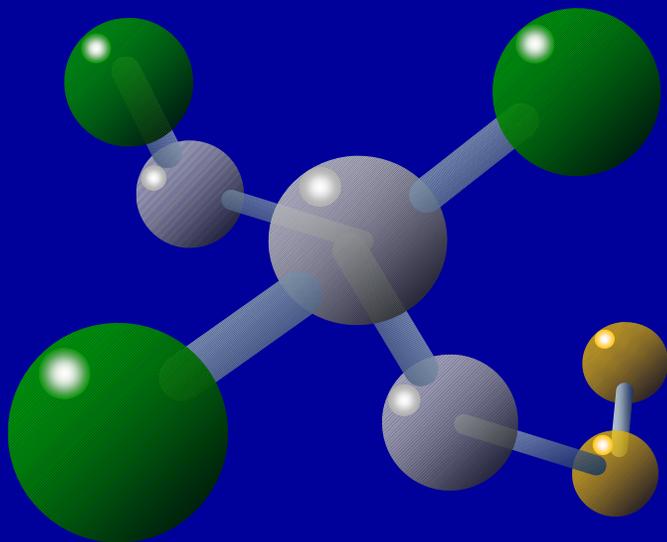
Это упрощенная
молекула **аллергена**,
например, сорняка.

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

Карбамилированный Аллергоид

The Carbamylated Allergoid

Это упрощенная молекула **аллергоида** - химически модифицированного **аллергена**.



Аллергоид получается в результате реакции карбамилирования циановокислым калием при щелочной рН, что приводит к значительному замещению аллерген лизиновых аминокрупп:

четко определенное основное действующее вещество.

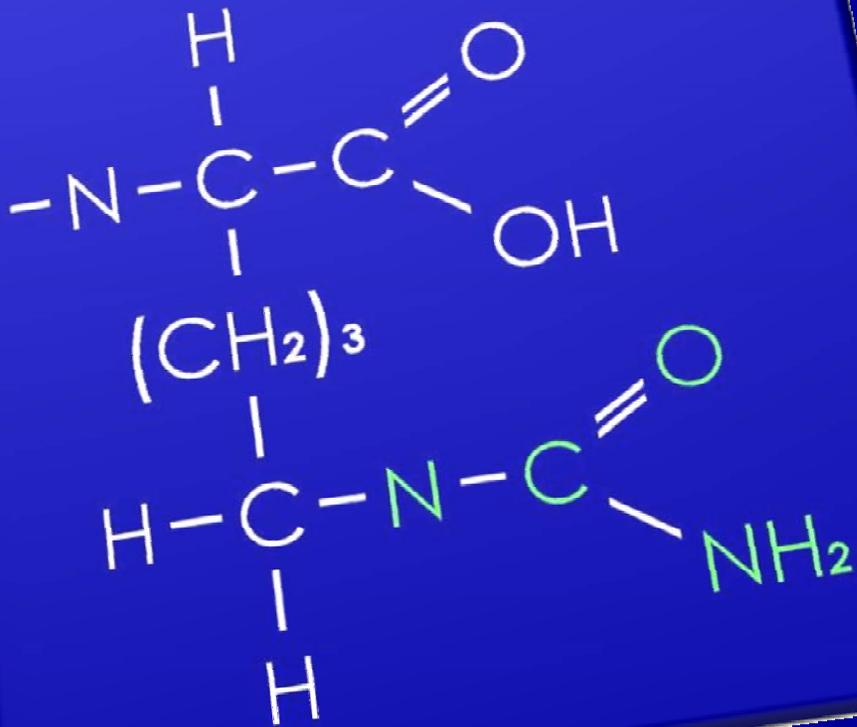
This is a simplification of an **allergoid** molecule, a chemical modification of an **allergen**.

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.

Каковы эффекты?

what are the consequences ?

Carbamylated Allergoid



1

**Резкое снижение
связывания
специфического IgE**

Dramatic reduction
of specific IgE linking

**Сниженная аллергенная
активность**
reduced
allergenic activity



БЕЗОПАСНОСТЬ
SAFETY

Каковы эффекты?

what are the consequences ?

2

Устойчивость к ферментативному расщеплению

Resistance to enzymatic degradation

Карбамилированный аллергоид остается АКТИВНЫМ

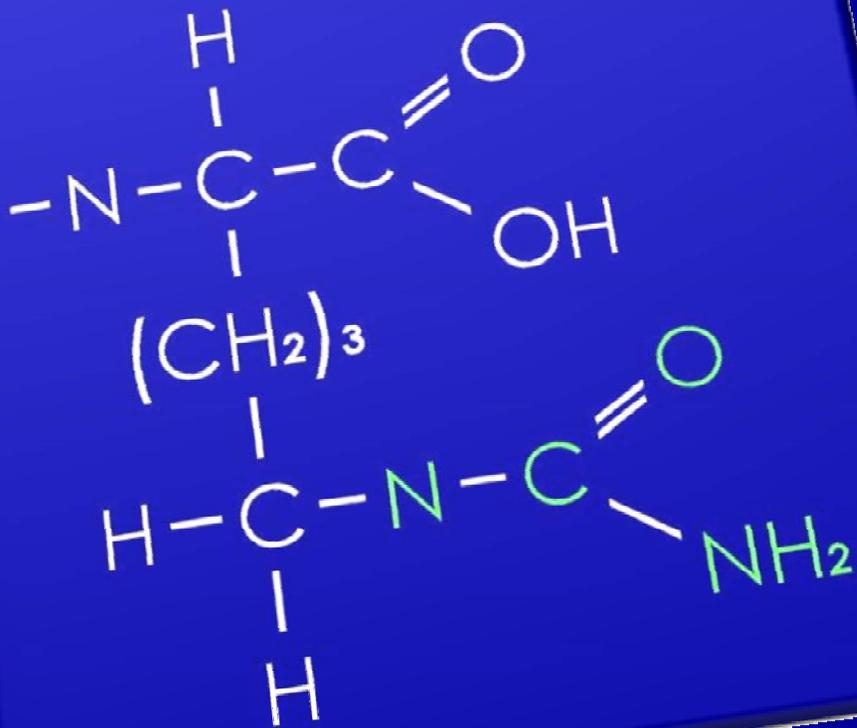
carbamylated allergoid remains active

**Нет потребности в *больших дозах*
Маленькие дозы - ЭФФЕКТИВНЫЕ ДОЗЫ**

"high doses" are not necessary.

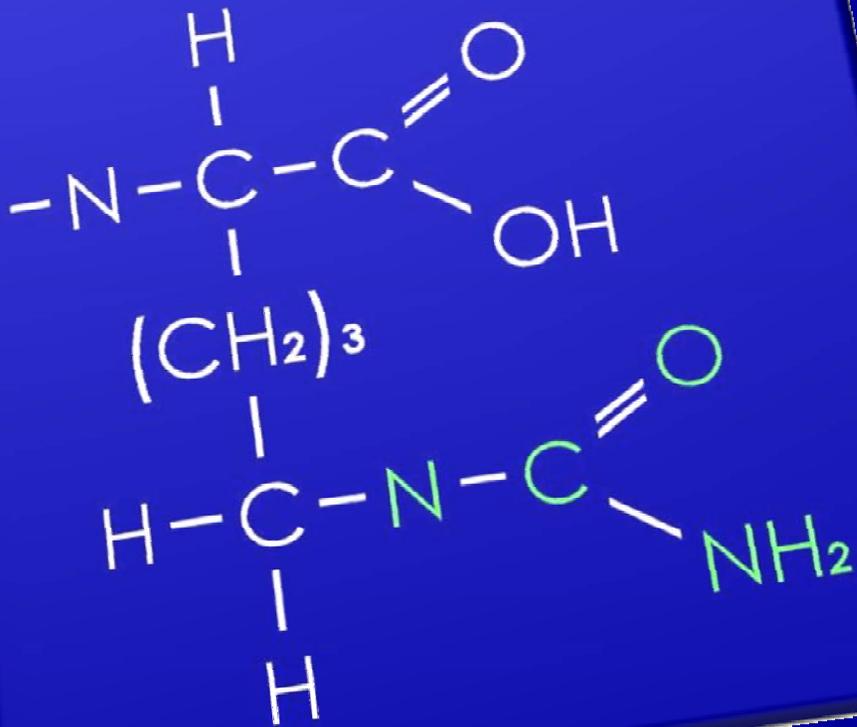
EFFECTIVE DOSES

Carbamylated Allergoid



Каковы эффекты? what are the consequences ?

Carbamylated Allergoid



3

Неизменяемость Т-клеточных эпитопов

NO
alteration of T-epitopes

Сохранение иммуногенной активности

preserved
immunogenic activity

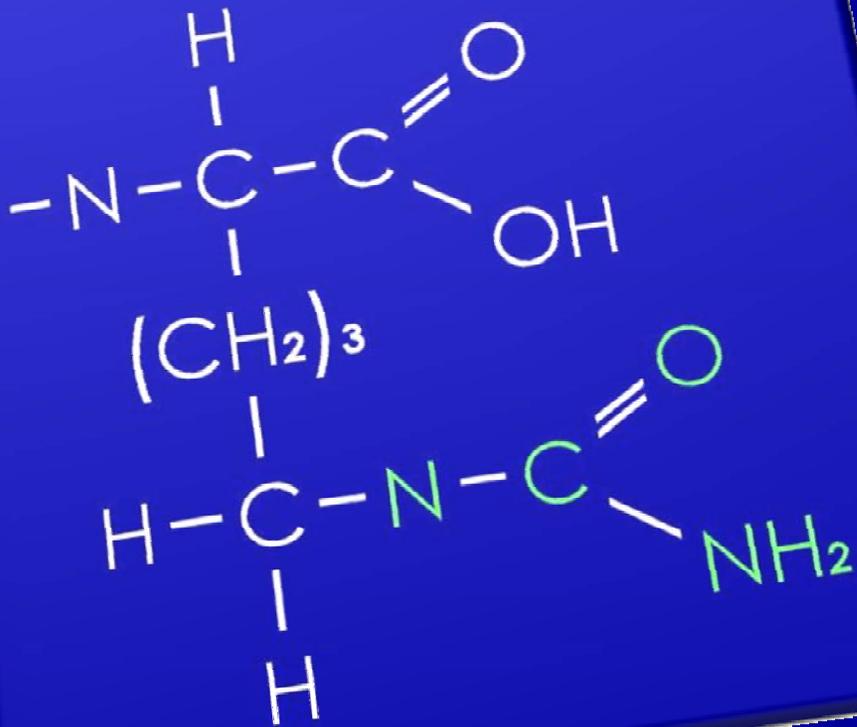


ЭФФЕКТИВНОСТЬ
EFFICACY

Каковы эффекты?
what are the consequences ?

4 Сохранение
молекулярных размеров

Carbamylated Allergoid



PRESERVATION
of molecular sizes

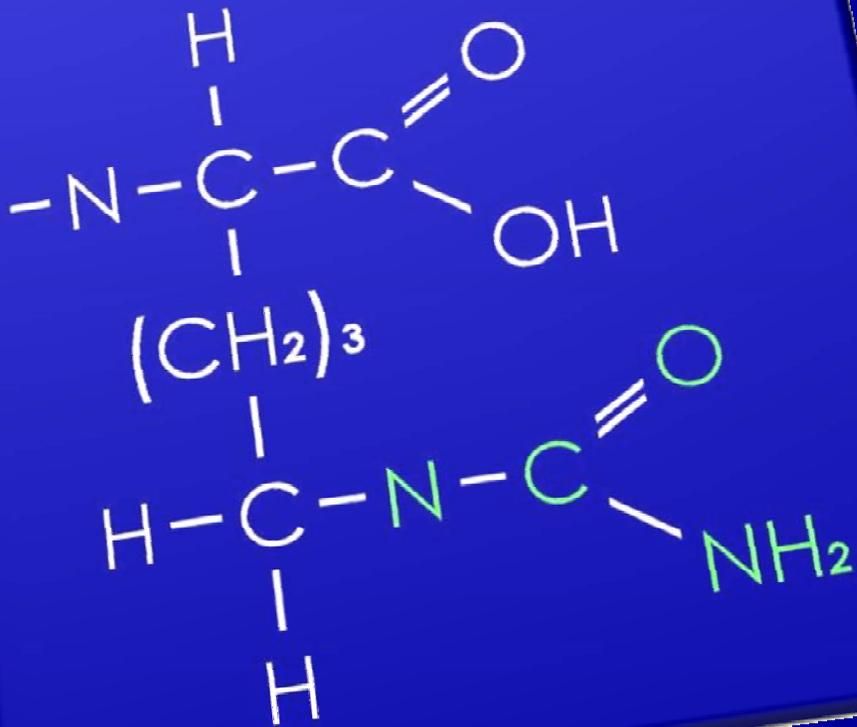
Карбамилированный Аллергоид
является Мономерным
Аллергоидом

Carbamylated Allergoid is
a Monomeric Allergoid

Подходит для
сублингвальной
иммунотерапии
FIT for SLIT

Каковы эффекты? what are the consequences ?

Carbamylated Allergoid



НЕОБРАТИМОСТЬ карбамилрования

5

IRREVERSIBILITY
of carbamylation

**Нативный аллерген не
восстанавливается**

NO back to
native allergen

**БЕЗОПАСНОСТЬ
SAFETY**

Отдельные случаи исследования

selected references

Synopsis of published Lais studies

Part 1: study design

AUTHOR	JOURNAL	Study	Adults/ Children	No. Patients	Diseases*	Allergen	Treatment	Tablets/Drops
Bordignon	Giorn It 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;351:829-32	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 2008;36(2):79-84	open	adults	65 (24A+21A+21C)	R and/or A	Parietaria	co-seasonal	Tab
Lombardi	Allergy 2001;56:989-992	open (safety)	adults	198	R and/or A	Mites(20), Grass(75), Olive(1), birch(4), Parietaria(46)	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)	continuous	Tab
Rossi	Giorn It 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(20), 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 co+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+30Chiev) 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-Rhinitis; A = Asthma; C = Conjunctivitis; RC = Rhino-Conjunctivitis

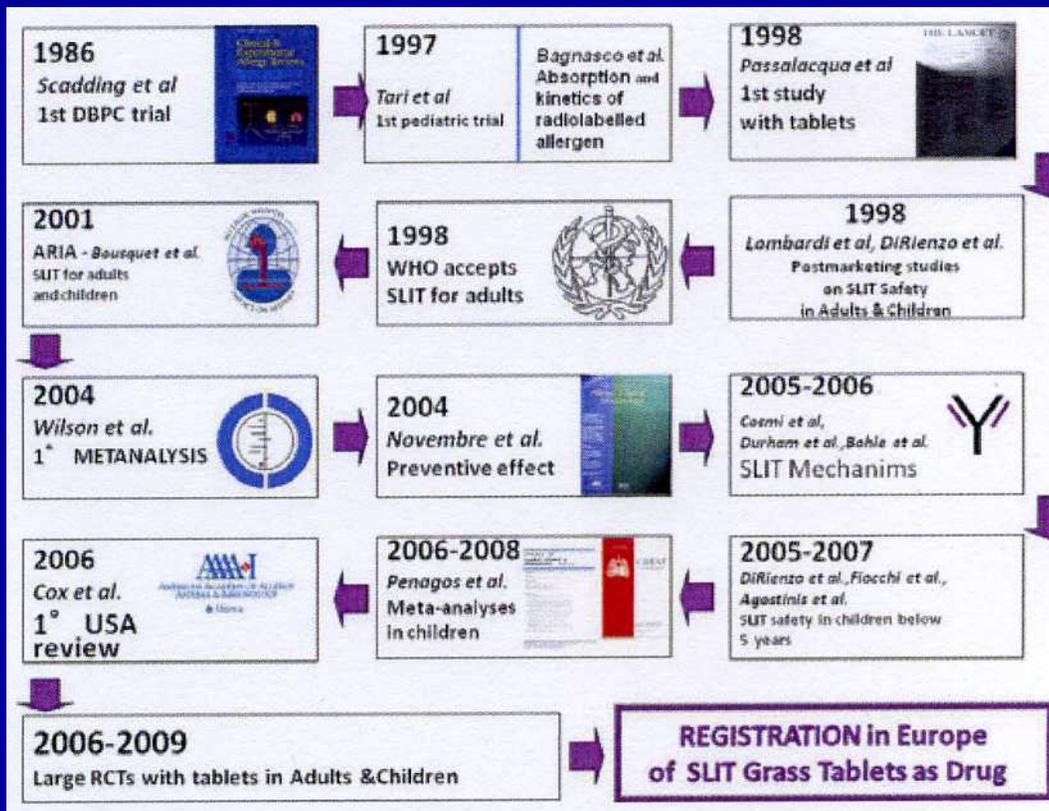
Synopsis of published Lais studies

Part 2: results

AUTHOR	JOURNAL	Treatment		Results Symptoms	Results Drugs	Results Mch	Cumulative dosages in AU/year
		Build up	Maintenance AU				
Bordignon	Giorn It 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;351:829-32	14 weeks	4000/week	reduction	reduction	reduction CMAI, 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
Gosmi	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 2008;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	Giorn It 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 9 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

Описание карбамиллированного аллергоида в истории SLIT

The contribution of carbamylated allergoid
in the history of SLIT



1997
Bagnasco, JACI

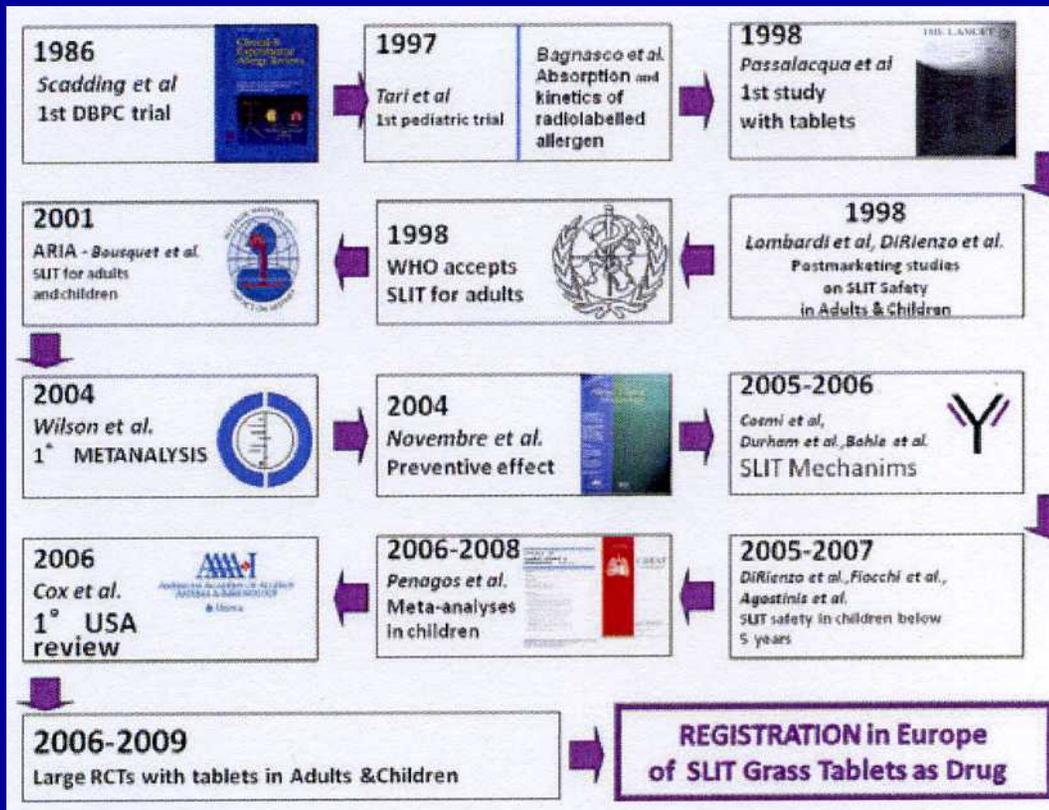
Первое кинетическое
исследование

1997
Bagnasco, JACI

1st study on
kinetics

Описание карбамиллированного аллергоида в истории SLIT

The contribution of carbamylated allergoid
in the history of SLIT



1998
Passalacqua, Lancet

Первое исследование
применения таблеток,

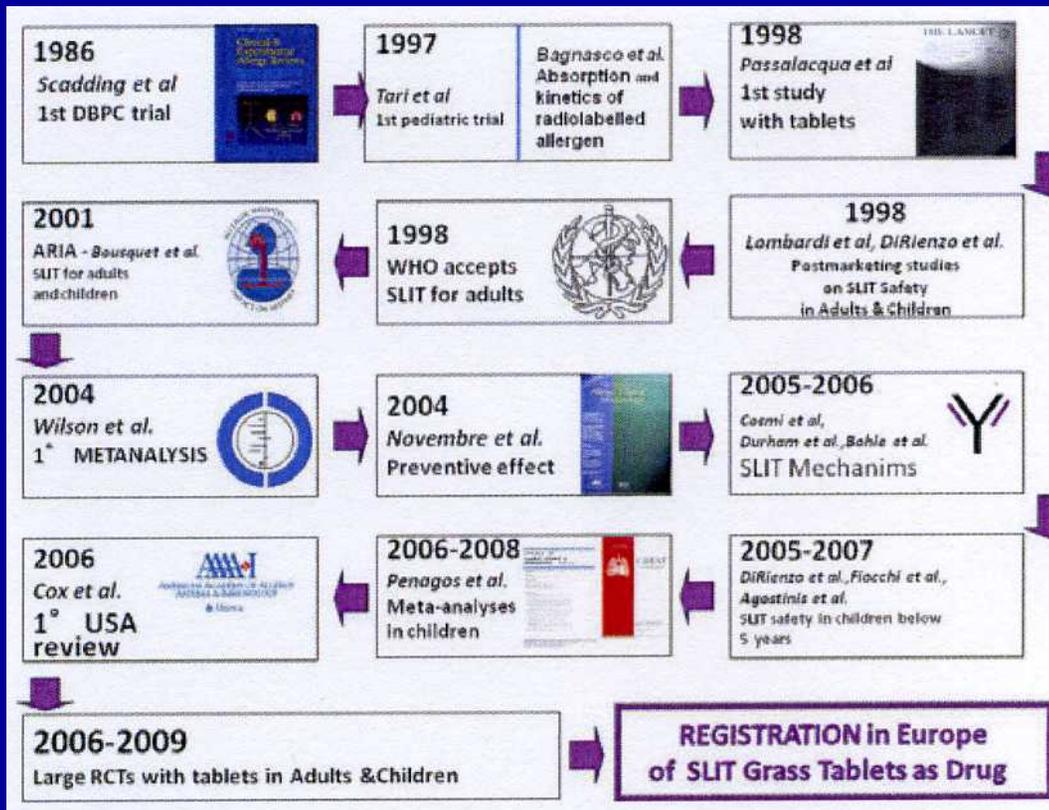
аллергоиды в
таблетках

1998
Passalacqua, Lancet

1st study with
tablets,
allergoid tablets

Описание карбамиллированного аллергоида в истории SLIT

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in the history of SLIT



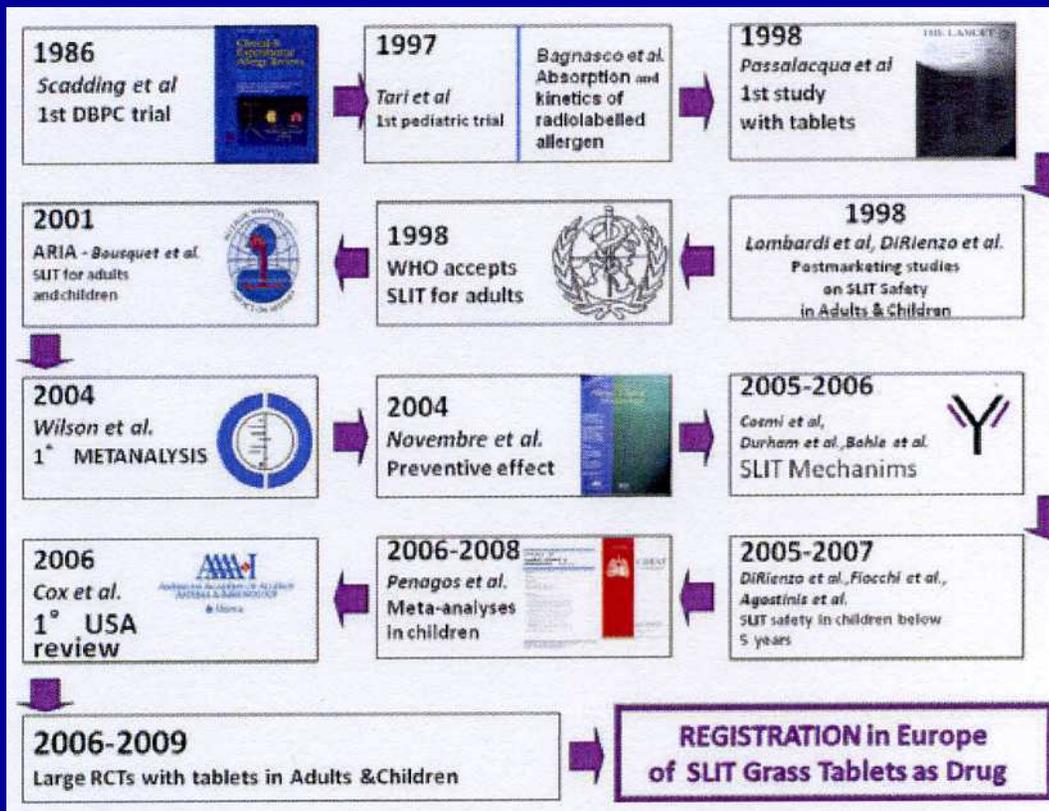
2000
Caffarelli, Allergy

Первое исследование
таблеток
на детях

2000
Caffarelli, Allergy
1st study with
tablets
in children

Описание карбамилированного аллергоида в истории SLIT

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in the history of SLIT



2001
Bagnasco, Allergy

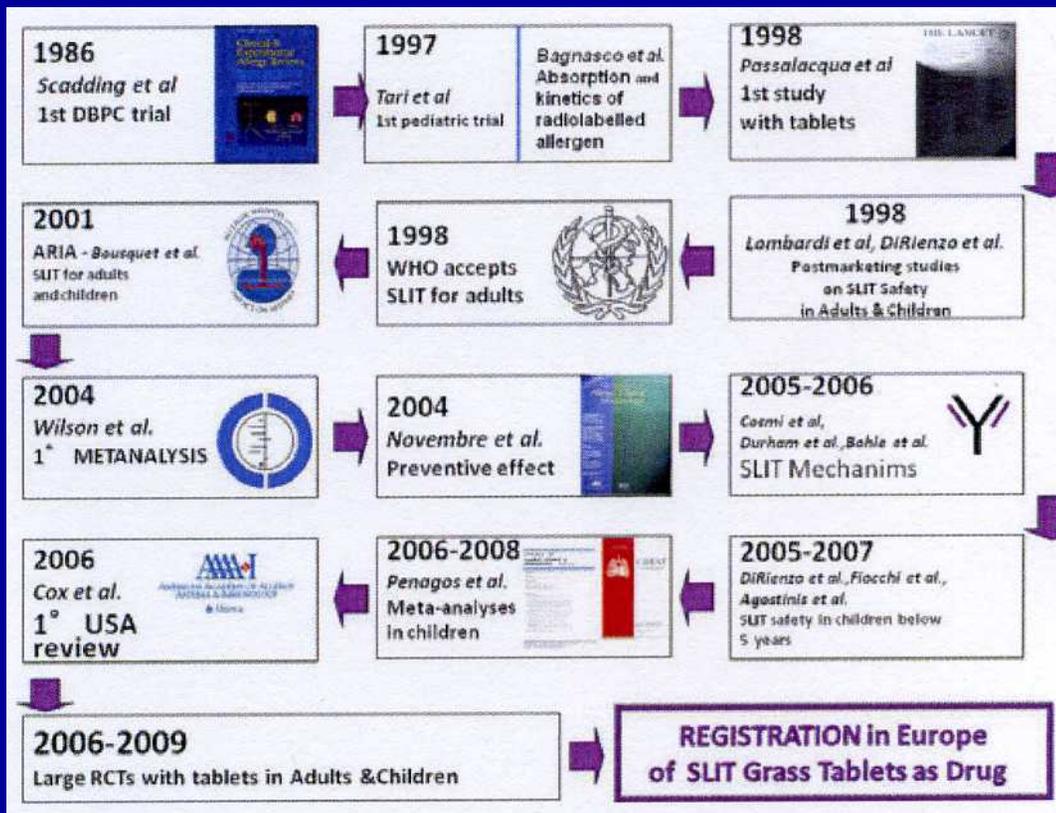
Сравнение между
аллергоидами в таблетках
и аллергенами в таблетках и
растворе

2001
Bagnasco, Allergy

Comparison between
allergoid tablets
vs
allergen in tablets
and in solution

Описание карбамиллированного аллергоида в истории SLIT

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in the history of SLIT



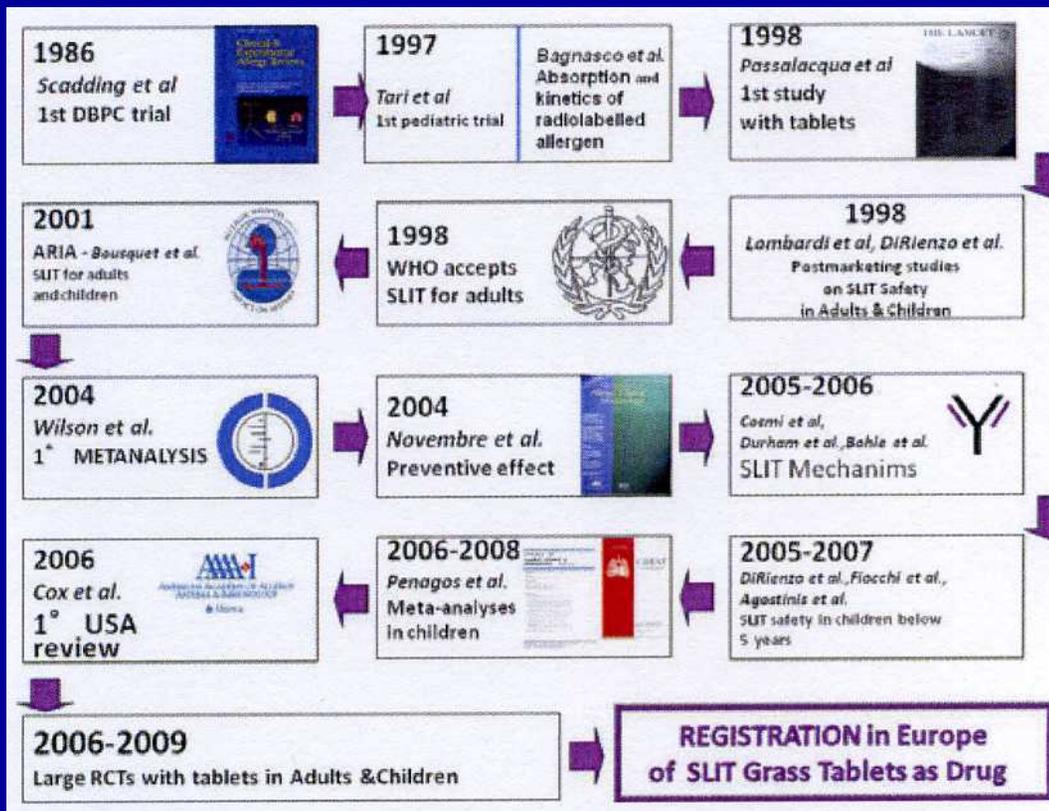
2001
Lombardi, JACI

Принципы аллергоид
сублингвальной
иммунотерапии

2004
Lombardi, JACI
Adherence
to allergoid SLIT

Описание карбамиллированного аллергоида в истории SLIT

The contribution of carbamylated allergoid
in the history of SLIT



2005
Agostinis, Allergy

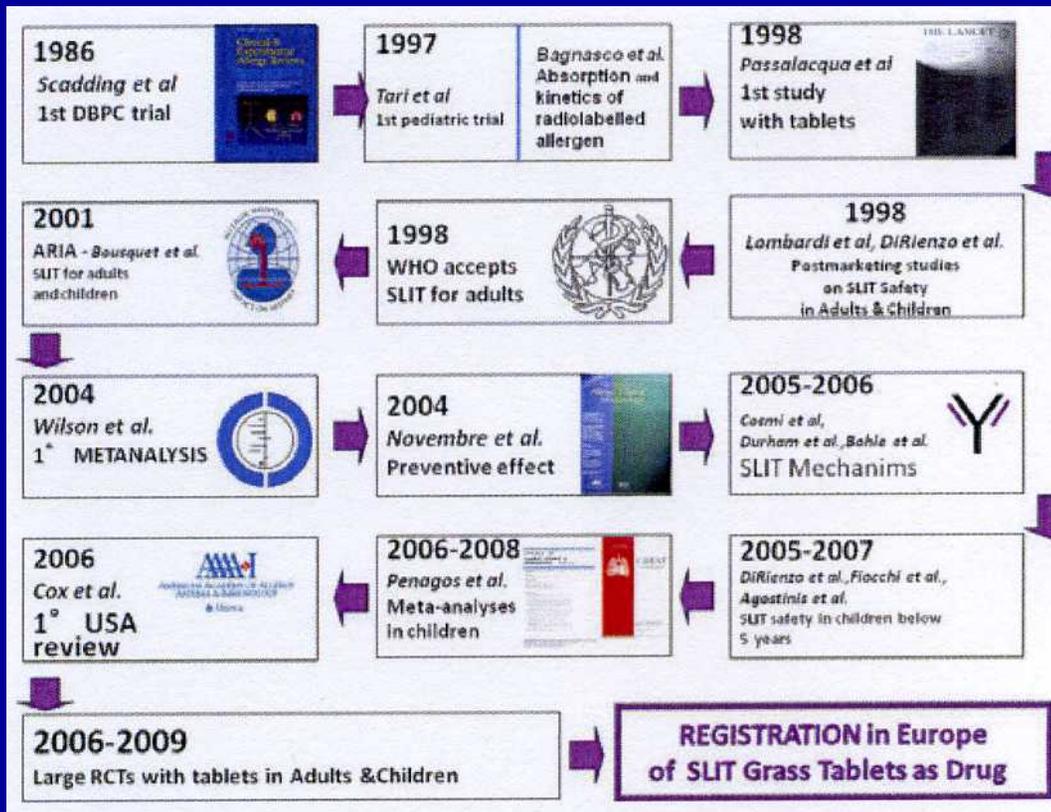
Безопасность для
детей

2005
Agostinis, Allergy

Safety
in children

Описание карбамиллированного аллергоида в истории SLIT

The contribution of carbamylated allergoid
in the history of SLIT



2006
Cosmi, Clin Exp Allergy

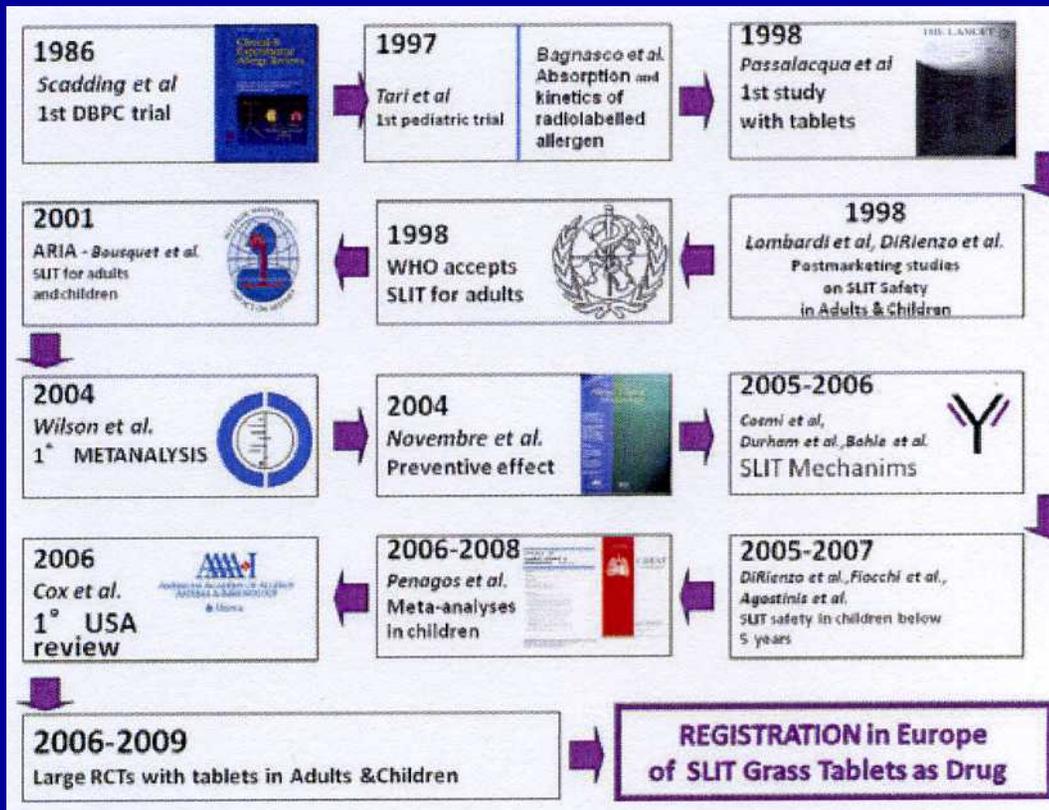
Механизм аллергоид
сублингвальной
иммунотерапии

2006
Cosmi, Clin Exp Allergy

Allergoid SLIT
mechanism

Описание карбамиллированного аллергоида в истории SLIT

The contribution of carbamylated allergoid
in the history of SLIT



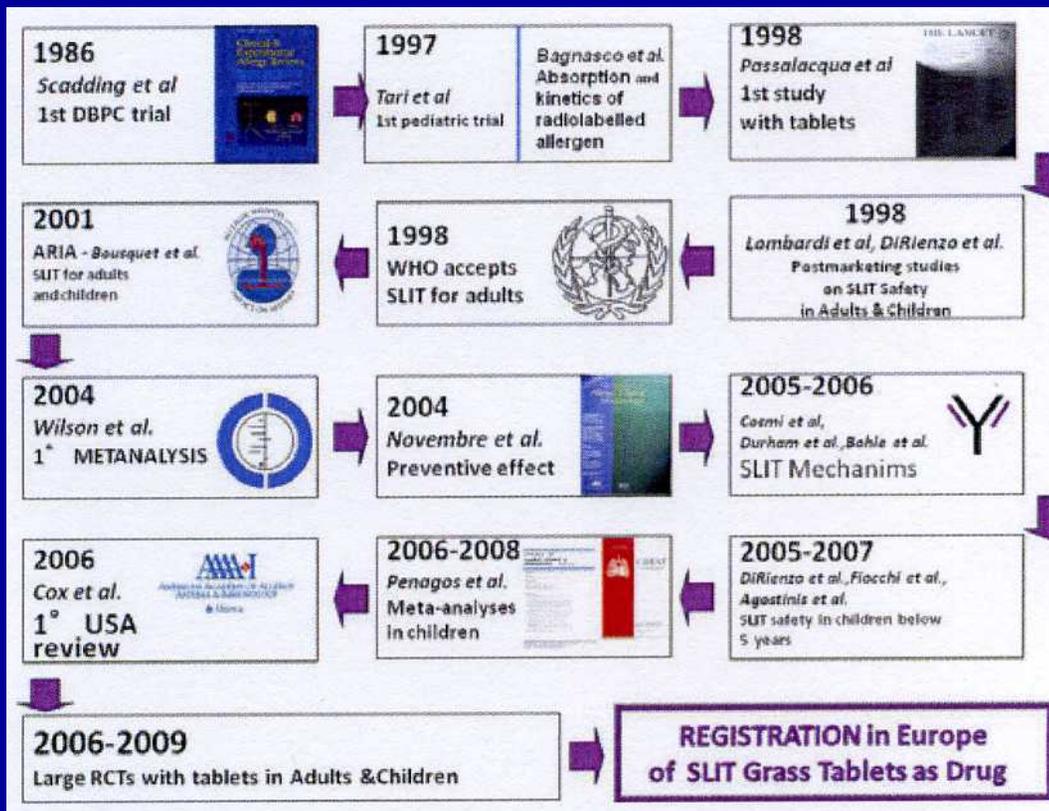
2009
D'Anneo, Int J Imm Pharm

Безопасность и
переносимость аллергоидной
SLIT с
4-дневной фазой
ИНДУКЦИИ

2009
D'Anneo, Int J Imm Pharm
Allergoid SLIT safety and tolerability with
4-day
induction phase

Описание карбамиллированного аллергоида в истории SLIT

The contribution of carbamylated allergoid
in the history of SLIT



2010
Passali, Acta ORL

Безопасность и
переносимость
аллергоидной SLIT
без фазы индукции

2010
Passali, Acta ORL

Allergoid SLIT safety and tolerability
without
induction phase

На рынке сегодня...

A final snapshot on the market...

Аллерген SLIT

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

Аллергоид SLIT

Allergoid SLIT

Lofarma - Lais tablets

Lofarma - Lais drops