VEQ Allergologia
Valutazione risultati VEQ ciclo 2016

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1* parte

VEQ ciclo 2016: valutazione risultati

V.E.Q.
ALLERGOLOGIA
Ciclo 2016

- 12 campioni di sieri liofili di origine umana
- Valutazione IgE specifiche per alimenti e inalanti
- Valutazione IgE totali

Centri partecipanti per Regione

118 Laboratori Ciclo 2016

-8 laboratori rispetto al 2015

126 Laboratori Ciclo 2015

129 Laboratori Ciclo 2014

INALANTI=10

Ambrosia
Bambagiona
Betulla
Olivo
Cipresso
Assenzio
Acaro della polvere
Cane
Gatto
parietaria

ALIMENTI N=12

Uovo
arachidi
grano
Soia
Pomodoro
Aglio
Cipolla *
Mela
Gambero
pesce
Nocciola
Mandorla*

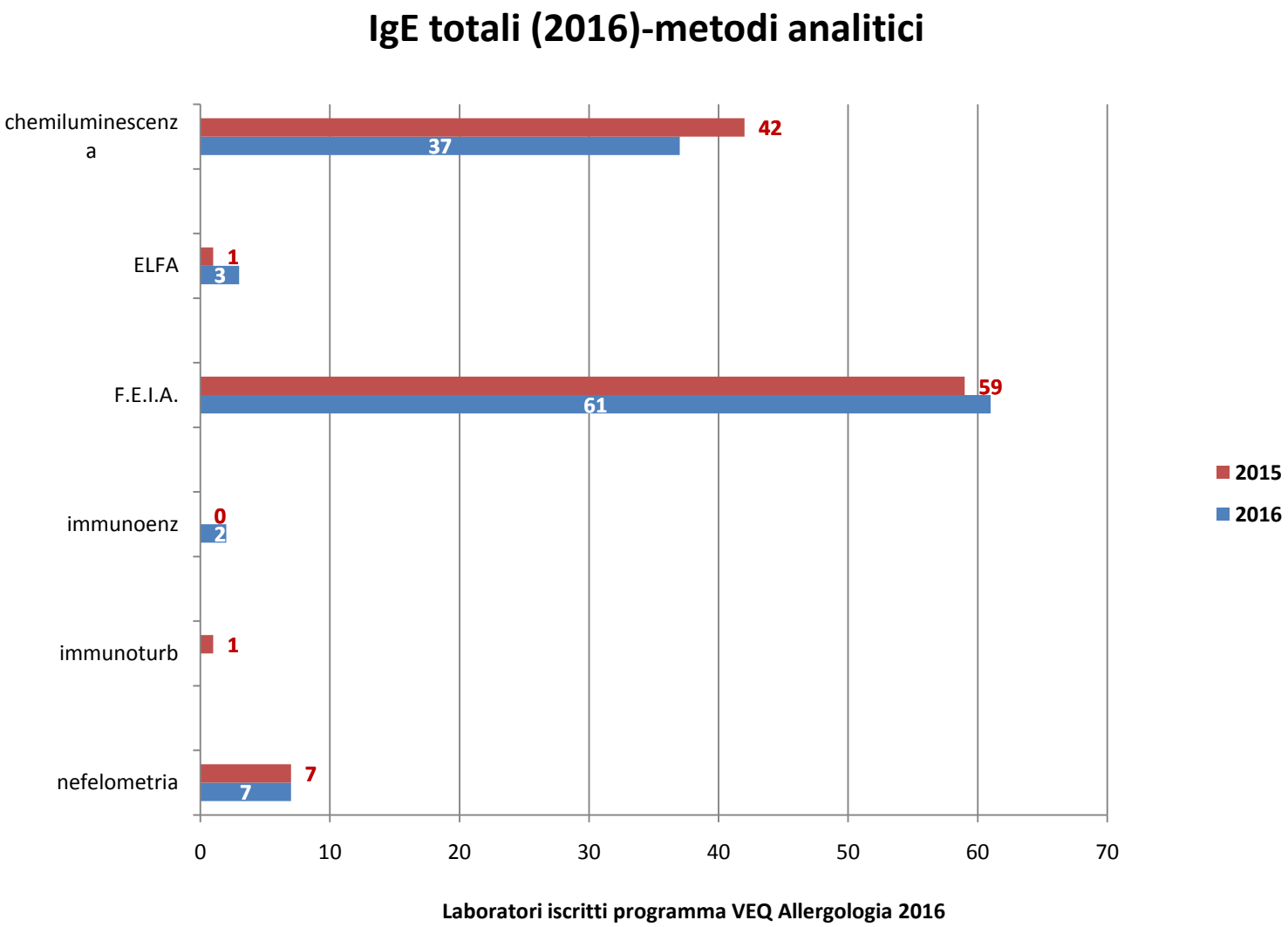
ALTRI ALLERGENI=2

Latex
Vespula*

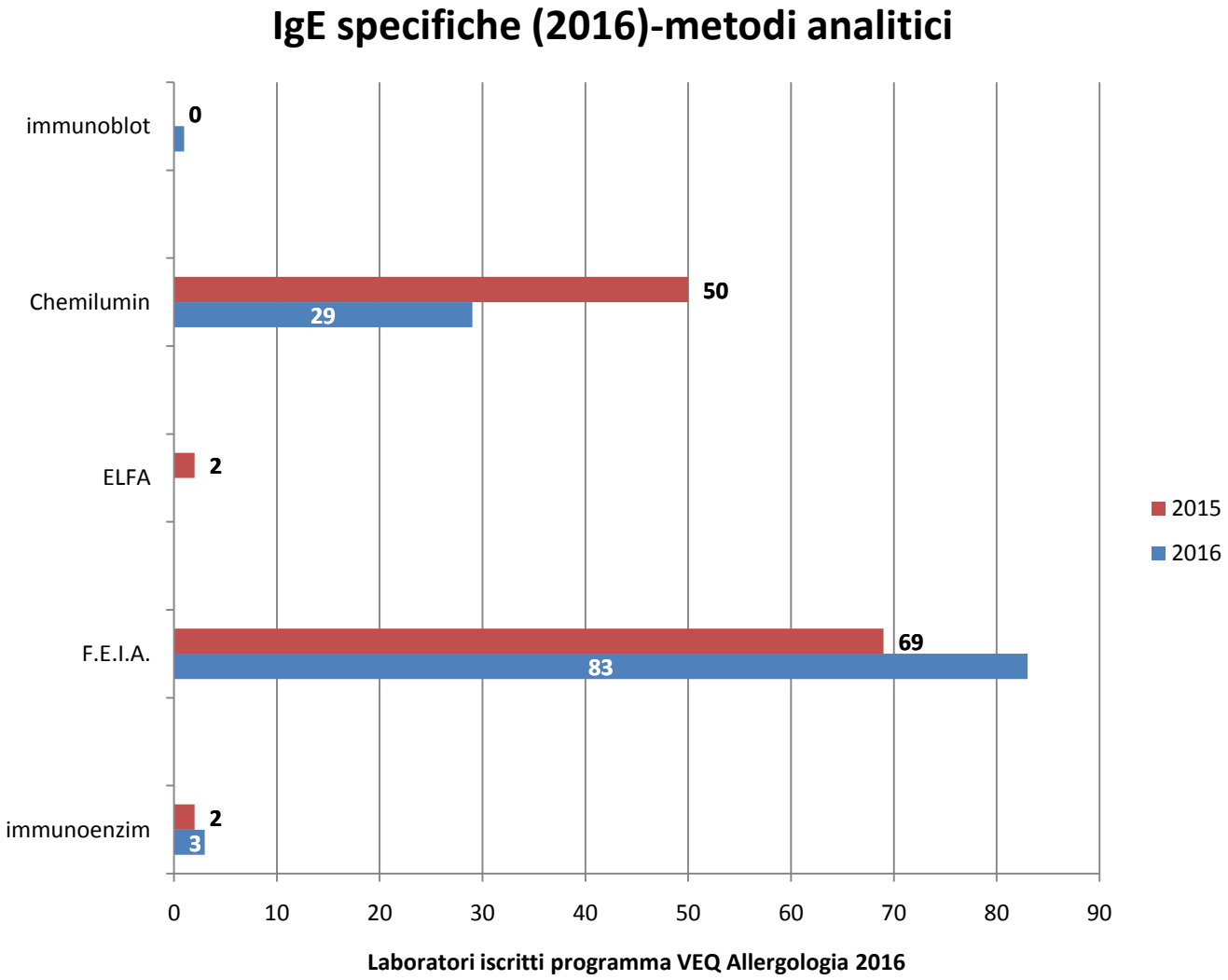
2016: 24 allergeni
2015: 21 allergeni

	1	2	3	4	5	6	7	8	9	10	11	12	N° dosaggi
Bianco d'uovo						x							1
Grano					x			x			x		3
Arachidi	x		x			x		X				x	5
Soia								X			x		2
Ambrosia								x					1
Pomodoro		x		x					x	x		X	5
Aglio											x	x	2
Mela	x			x		x	x		x			x	6
Cipolla			x			x							2
Bambagiona		x		x		x	x		x				5
Betulla verrucosa					x		x						1
Olivo		x		x		x		X			x		5
Cipresso medit.	x		x				x		x	x			5
Assenzio selvatico			x			x		x	x				4
D. pteronyssinus	x		x			x	x					x	5
Epitelio di gatto		x			x					x		x	4
Forfora di cane	x		x			x			x	x			5
Nocciole	x	x		x						x			4
Lattice					x			X			x		3
Parietaria judaica		x		x							x	x	4
Gambero	x				x		x						3
Pesce			x							x			2
Mandorle		x			x								2
Vespula					x								1
N° all. x Camp.	7	7	7	7	7	9	8	7	6	6	6	7	81

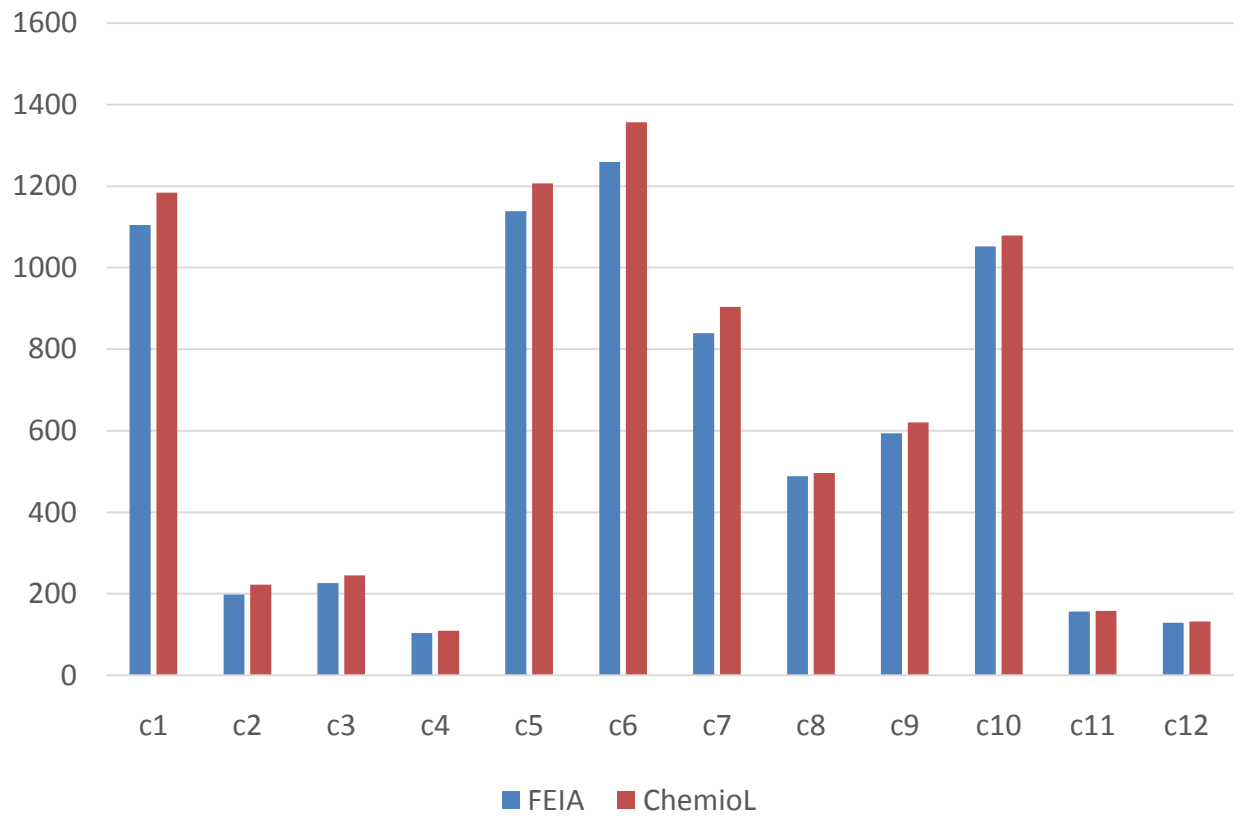
IgE Totali (2016) - metodi analitici



IgE Specifiche (2016) - metodi analitici



IgE Totali (2016) - medie

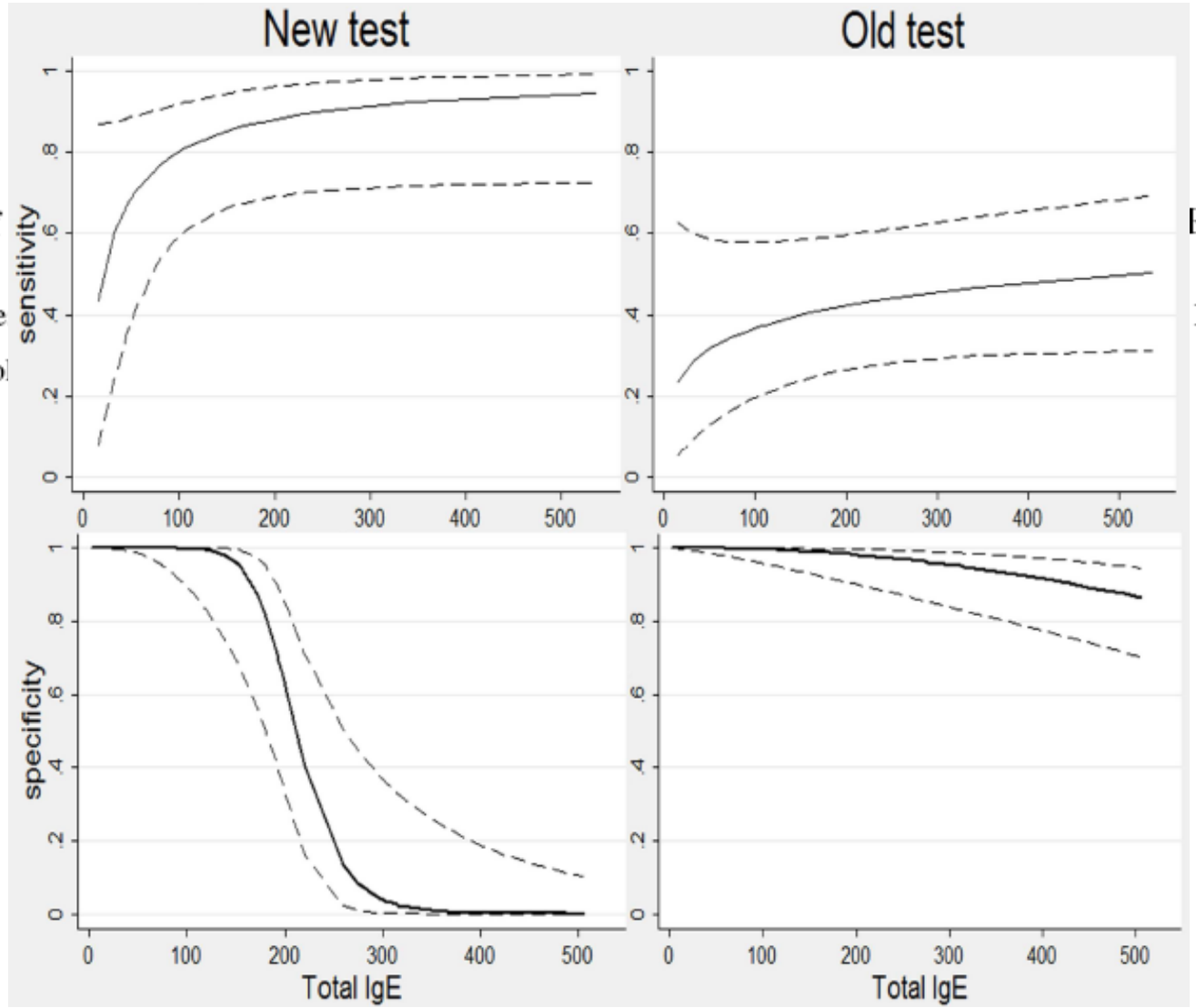


Interferenza da parte delle IgE totali

Influence of **E antibodies**

Vultaggio Ale Lucia BSc°,

Parronchi Pao



Exp All. (2009)

campione	alimenti		inalanti	
	ChemioL	FEIA	Chemio L	FEIA
#1 (nocciola/acaro)	neg	1.6 ± 0,1	45.6 ± 4.9	29 ± 3,2
#2 (pomodoro/gatto)	0,14 ± 0.03	1.4 ± 0.2	50.8 ± 5.79	24.3 ± 1.9
#3 (arachidi/cane)	0.55 ± 0.07	1.3± 0.2	3.2 ± 0.3	2.9 ± 0.25
#4 (mela/parietaria)	1.01 ± 0.08	0.61 ± 0.1	25.4 ± 2.4	13.9 ± 1.1
#5 (gambero/gatto)	Neg	3.2 ± 0.3	2.33 ± 0.22	0.88 ± 0.11

Nuovi allergeni

	Chemioluminescenza	FEIA
Vespula	13.4 ± 1.1	4.2 ± 0.35
	1 negativo	9 mancanti

	Chemioluminescenza	FEIA
Mandorle	1.54 ± 0.16	1.09 ± 0.28
	Concordanza del 100%	

IgE specifiche: quale significato clinico?

- Aumentando la concentrazione di IgE specifiche aumenta il grado di severità di manifestazione clinica (sia per inalanti che alimenti)

- *Tuttavia….*

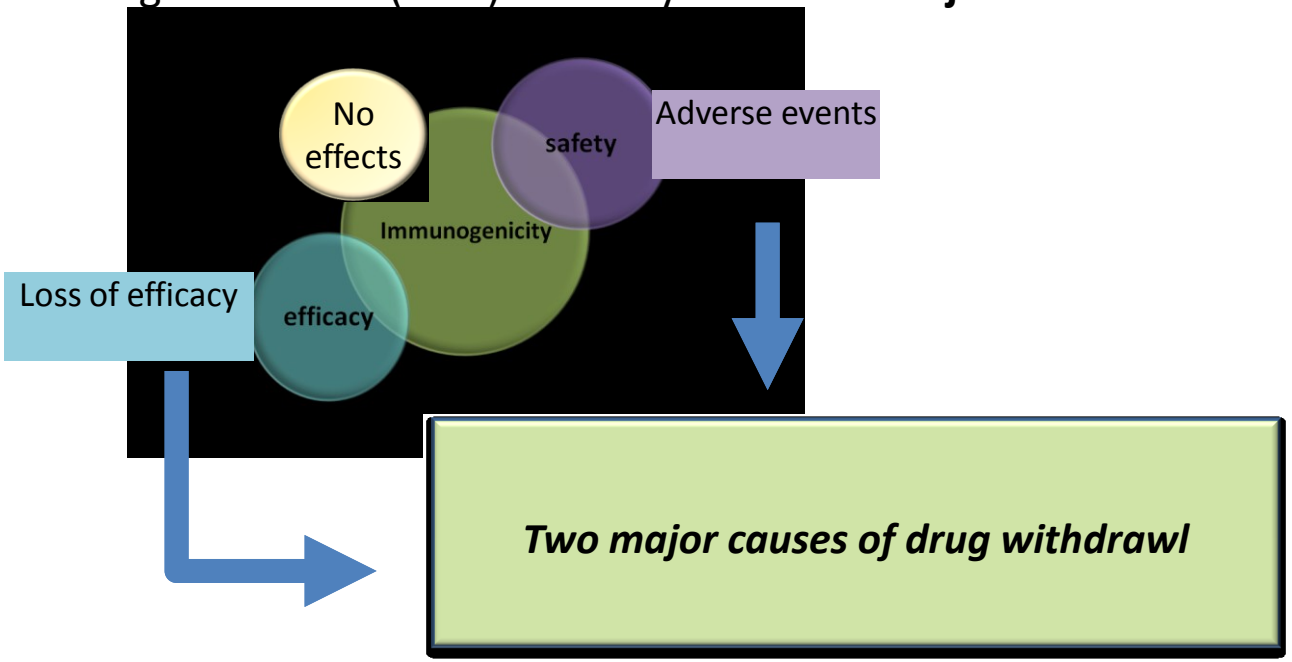
- Anche bassi valori di IgE specifiche per alimenti possono indurre anafilassi

2* parte

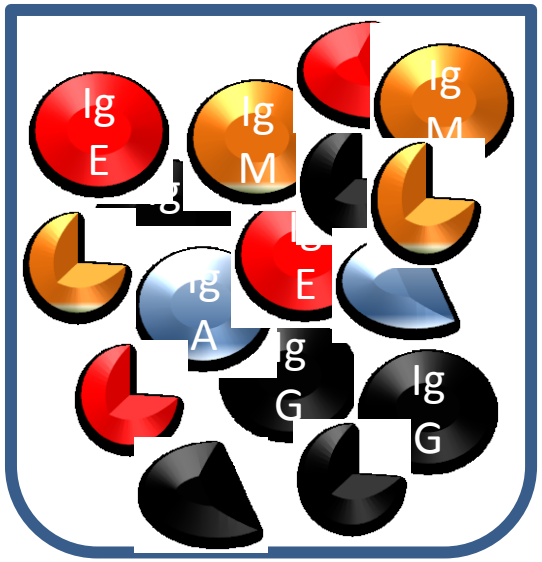
Immunogenicità dei farmaci biologici: luci ed ombre

Why are we interested to immunogenicity?

Unwanted immunogenicity leads to the development of anti-drug antibodies (ADA) and may have **two major clinical**



ADA: HETEROGENEITY IN COMPOSITION



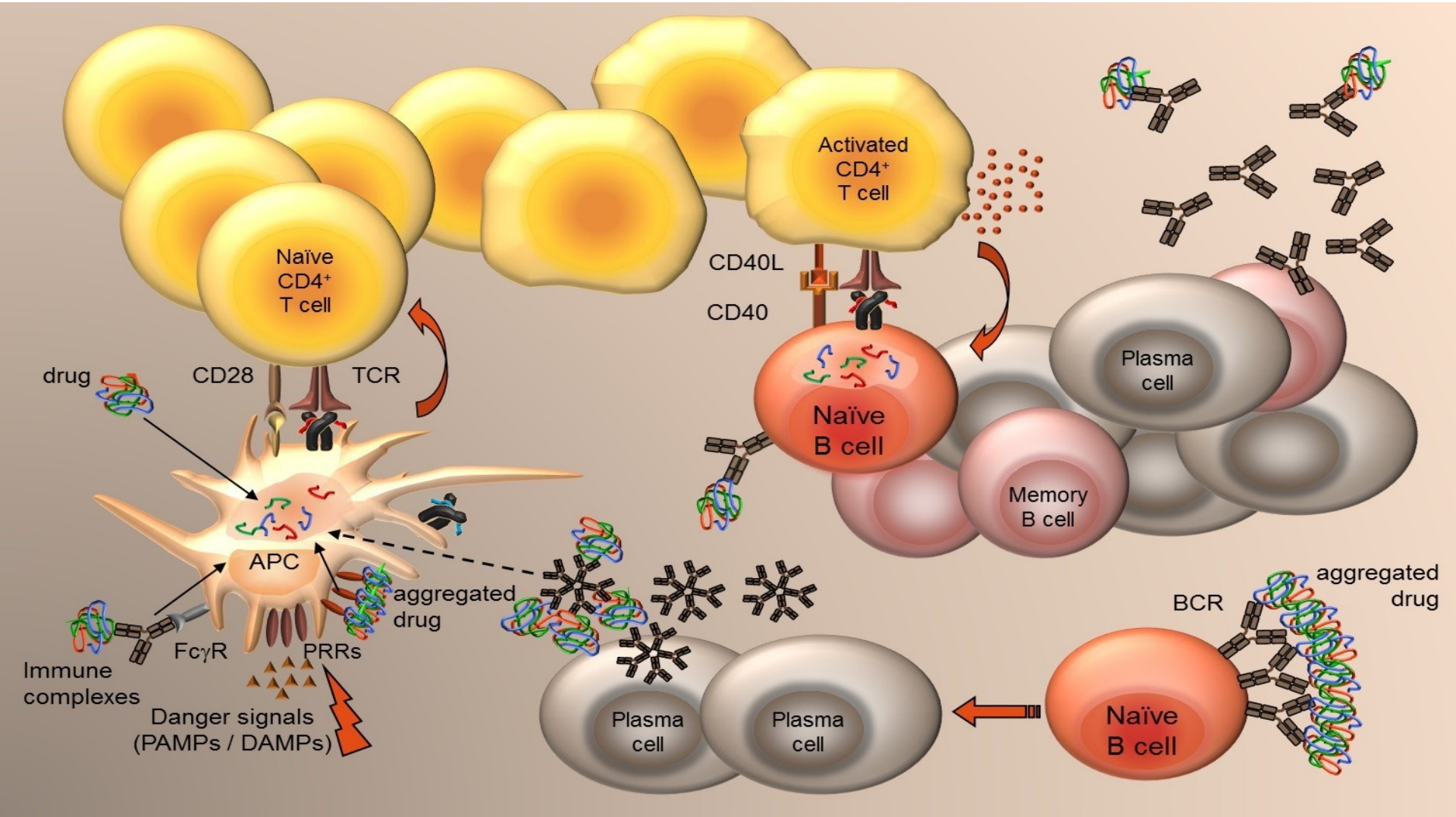
A mixture of different quantities of different:

- **Isotypes (IgG, IgA, IgM, IgE)**
- **Affinities (low, high)**
- **Specificities (idiotype, allotype, glycans)**

1. **Not all ADA+ patients develop ADA-related events**
2. **Not all ADA+ patients develop the same ADA-related event**

(Rup B et al, Clin Exp Immunol 2015)

Immunology behind immunogenicity of biologicals

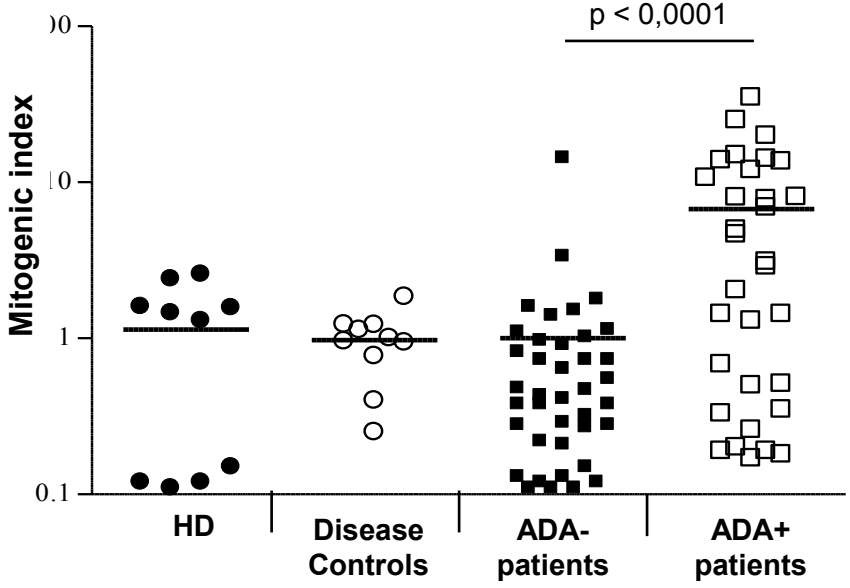


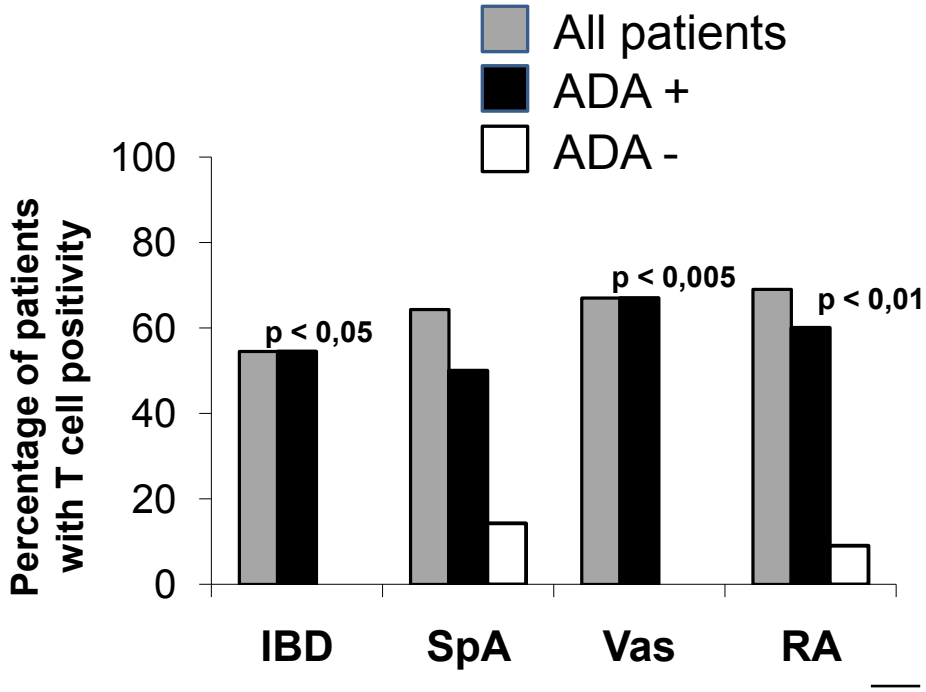
T cell positive response is mainly detectable in ADA+ patients in a disease-independent manner

a) 20/71 (**28.2%**) IFX-treated patients displayed a **proliferative cell response**

b) A significantly higher proportion of T cell positivity developed among **ADA+ patients (56.6%)** than in **ADA- patients (5.1%)**

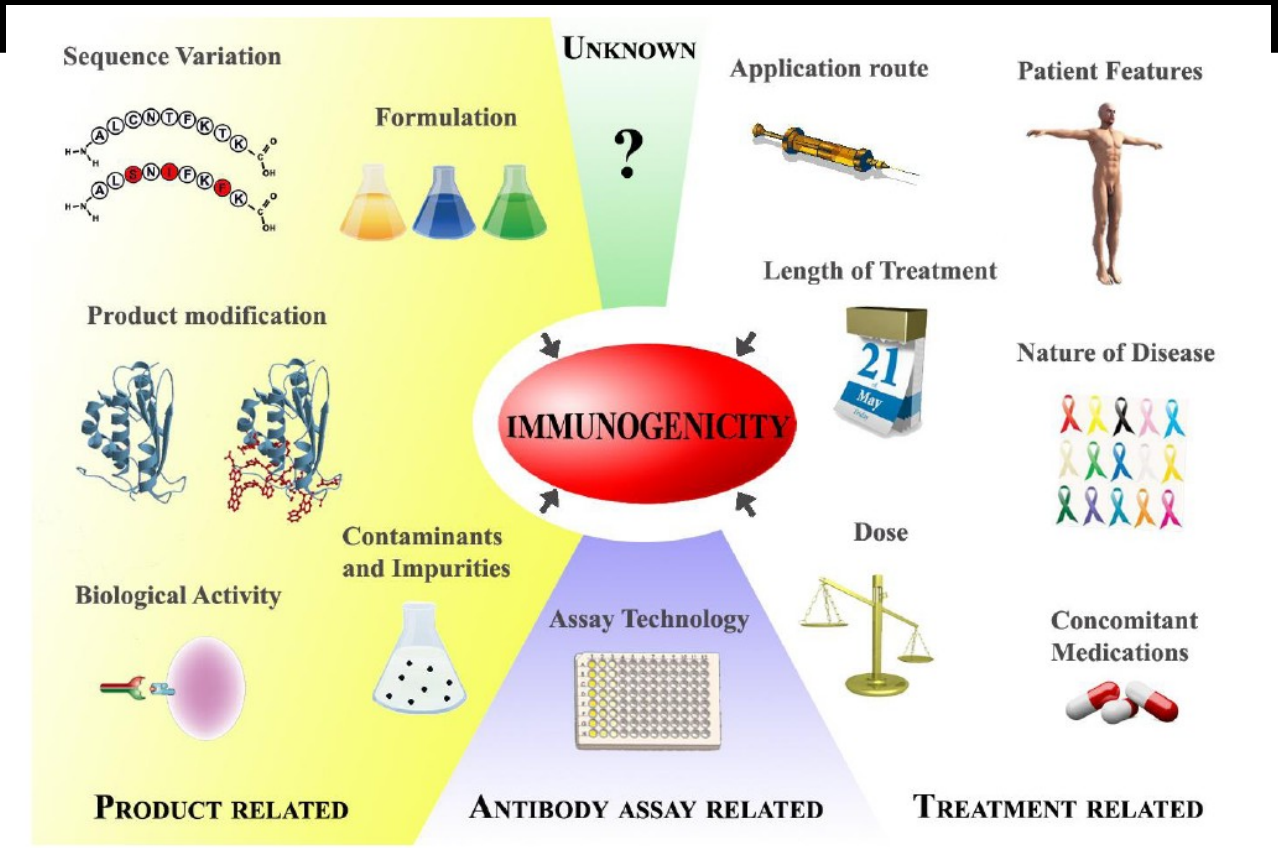
ADA status
N=39 ADA-
N=32 ADA+





(Vultaggio A et al, Clin Exp Immunol 2016)

Factors influencing immunogenicity

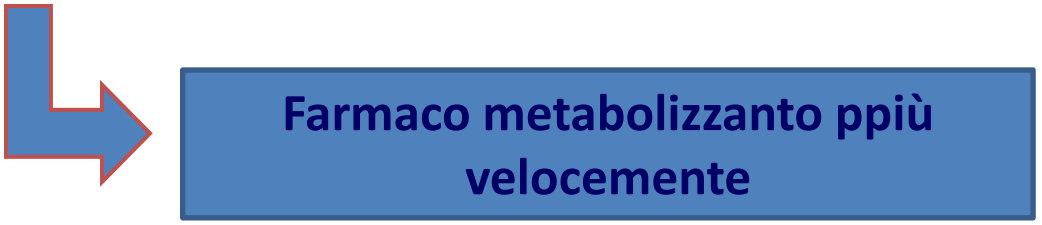


From Schellekens & Giovannoni 2003

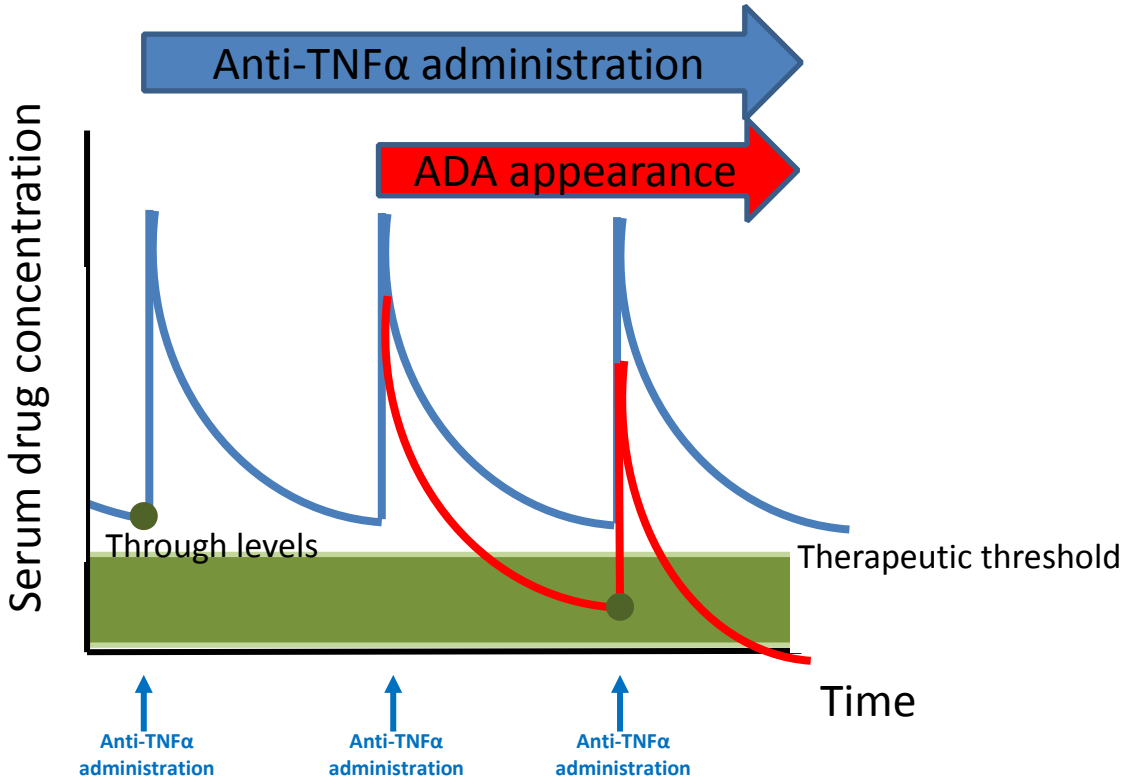
Immunogenicità come causa di perdita di efficacia dei farmaci biologici

1. **Anticorpi neutralizzanti: che prevengono l'azione del farmaco**

2. **Anticorpi cliranti: che incrementano la PK del farmaco**



ADA and pharmacokinetic of the drug

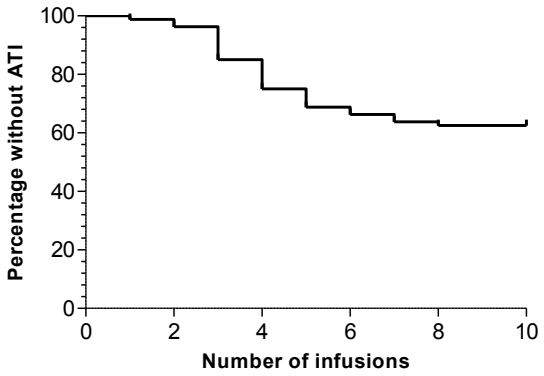


ATI ONSET IS AN EARLY EVENT THAT ANTICIPATES CLINICAL OUTCOMES

From 2007 to 2015, 91 IFX-treated patients were prospectively monitored (up to 40 infusions)* for ADA development and clinical outcome

[about 1200 serum samples evaluated]

* Serum collected before each infusion



- 45 % of IFX-treated patients developed ADA,
- Among ADA+ patients, the large majority of them (85%) developed ADA within the first 5 infusions (about 6 months)

	Time of drug negativization (weeks)	Time to first detection of ATI (weeks)	Time of onset of clinical outcome (weeks)
IBD (n=18)	23 ± 6	24 ± 4,8	31 ± 6
Arthritis (n=45)	19 ± 2,6	20 ± 3,7	42 ± 16
Vasculitis (n=28)	17,5 ± 1,9	27,3 ± 4	38,8 ± 10
Total	19,6 ± 1,9	23,2 ± 2,4	38,2 ± 8,3

(in preparation)

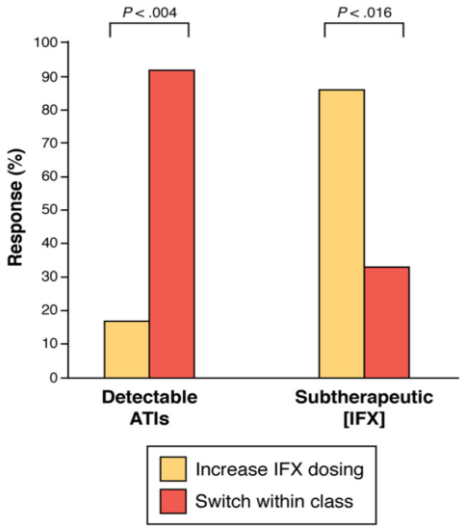
May immunogenicity drug monitoring help our therapeutic strategies?

If a patient becomes refractory:

1. ***Increase the dose or shorten the interval between doses***

2. ***Switch to another antiTNF (switch within class)***

3. ***Switch to another agent with a different action (switch out of class)***



Testing-based strategies showed to reduce overall
treatment costs by 50% (in IBD patients)

Afif W et al 2010

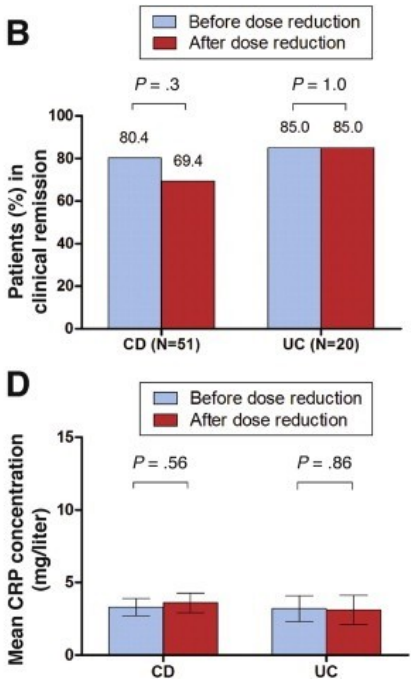
Steenhold et al 2014

May immunogenicity drug monitoring help our therapeutic strategies?

Guide treatment downscaling for patients in remission?

IFX-treated IBD patients

-27.9% costs saving!!



(Vande Casteele N et al, Gatroenterology 2015)

Towards optimal cut-off levels ?

Which is the therapeutic range?

1. **To be defined in further longitudinal wider studies**
2. **It is probably disease- and patient-dependent**
3. **It is probably assay-dependent**

Conclusioni

- Immunogenicità dei farmaci biologici è il risultato di una risposta immune completa
- Gli ADA possono negativamente influenzare la terapia con farmaco biologico
- Gli ADA anticipano l'evento clinico (perdita di efficacia/evento avverso)
- Vantaggi dell'appliacazione di strategie terapeutiche basate sullo studio della immunogenicità