



VEQ Allergologia

Valutazione risultati VEQ ciclo 2015

Alessandra Vultaggio

SOD Immunoallergologia

Dipartimento Medico-Geriatico

AOU Careggi

vultaggioa@aou-careggi.toscana.it

vultaggioalessandra@gmail.com





V.E.Q. ALLERGOLOGIA Ciclo 2015



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

Centri partecipanti per Regione

126 Laboratori Ciclo 2015

-3 laboratori rispetto al 2014

129 Laboratori Ciclo 2014

63 Laboratori Ciclo 2009



21 Allergeni dosati nel ciclo 2015

10 alimenti + 11 inalanti

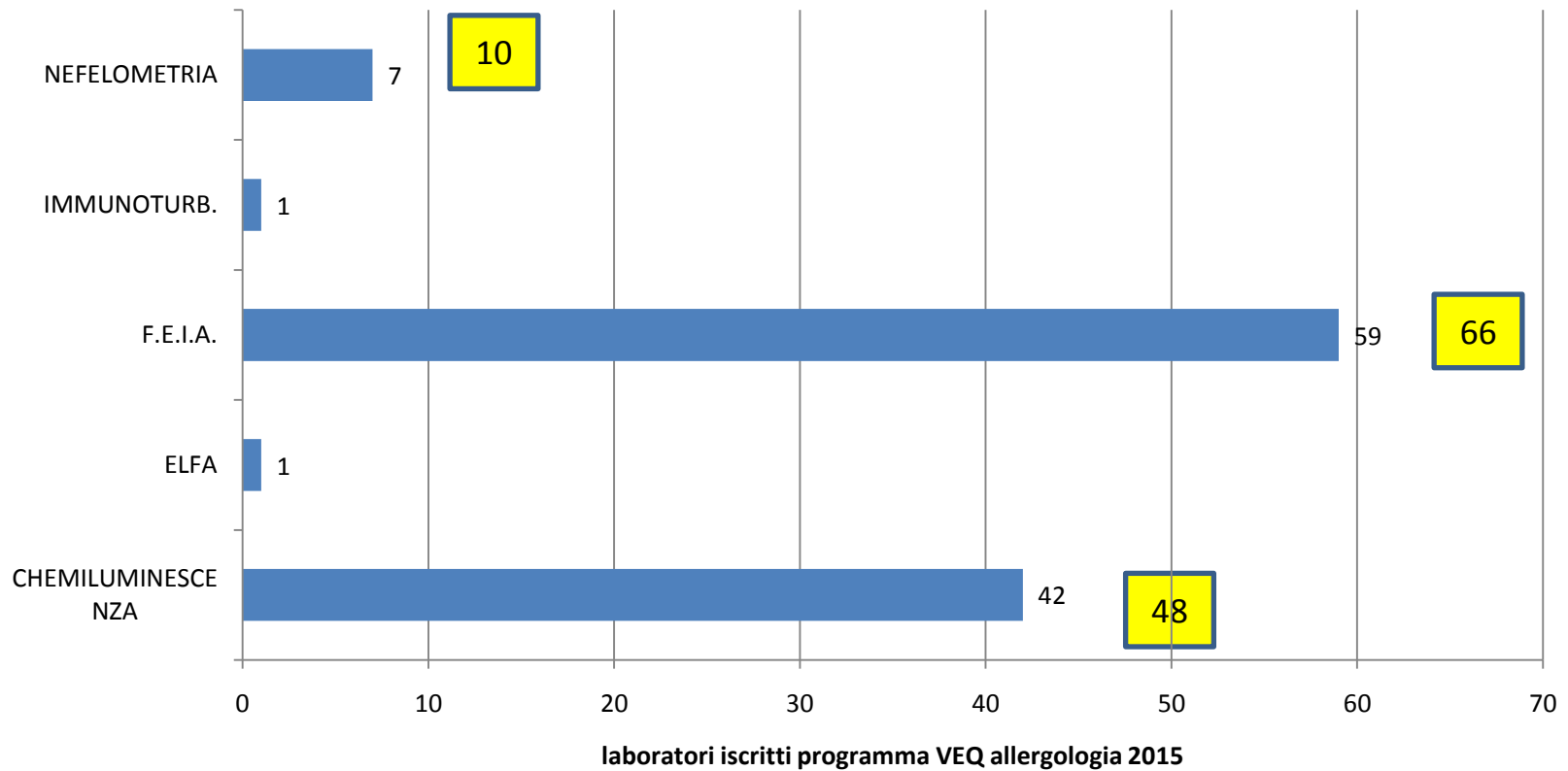
	1	2	3	4	5	6	7	8	9	10	11	12	N° dosaggi
Bianco d'uovo										X			1
Grano	X				x	X	x				X	x	6
Arachidi		X		X			x		X	X			5
Soia		X				X			X			x	4
Pomodoro	x				x	X	X					x	5
Aglio		X			x				x	X			4
Mela			x	X				X		X			4
Bambagiona	X							X			X		3
Betulla verrucosa		x		X				X			X	x	5
Olivo	X		X	X			X		X			x	6
Cipresso mediterr.	X			x			x	X					4
Artemisia folia				X	X	X			X				4
Assenzio selvatico		X	X		X					X	X	X	6
D. pteronyssinus	X					X		X		X		X	5
Epitelio di gatto	X							X		X			3
Forfora di cane			X										1
Nocciole		X		X			x	X		X			5
Lattice			X		x	X	x		X		x		6
Parietaria judaica			X		X				X		X		4
Gambero			x				x	X					3
Pesce						X					x		2
N° all. x Camp.	7	6	7	7	7	7	8	8	7	8	7	7	86

Forfora di cavallo **non** presente nel 2015 rispetto al 2014

IgE Totali (2015) - metodi analitici

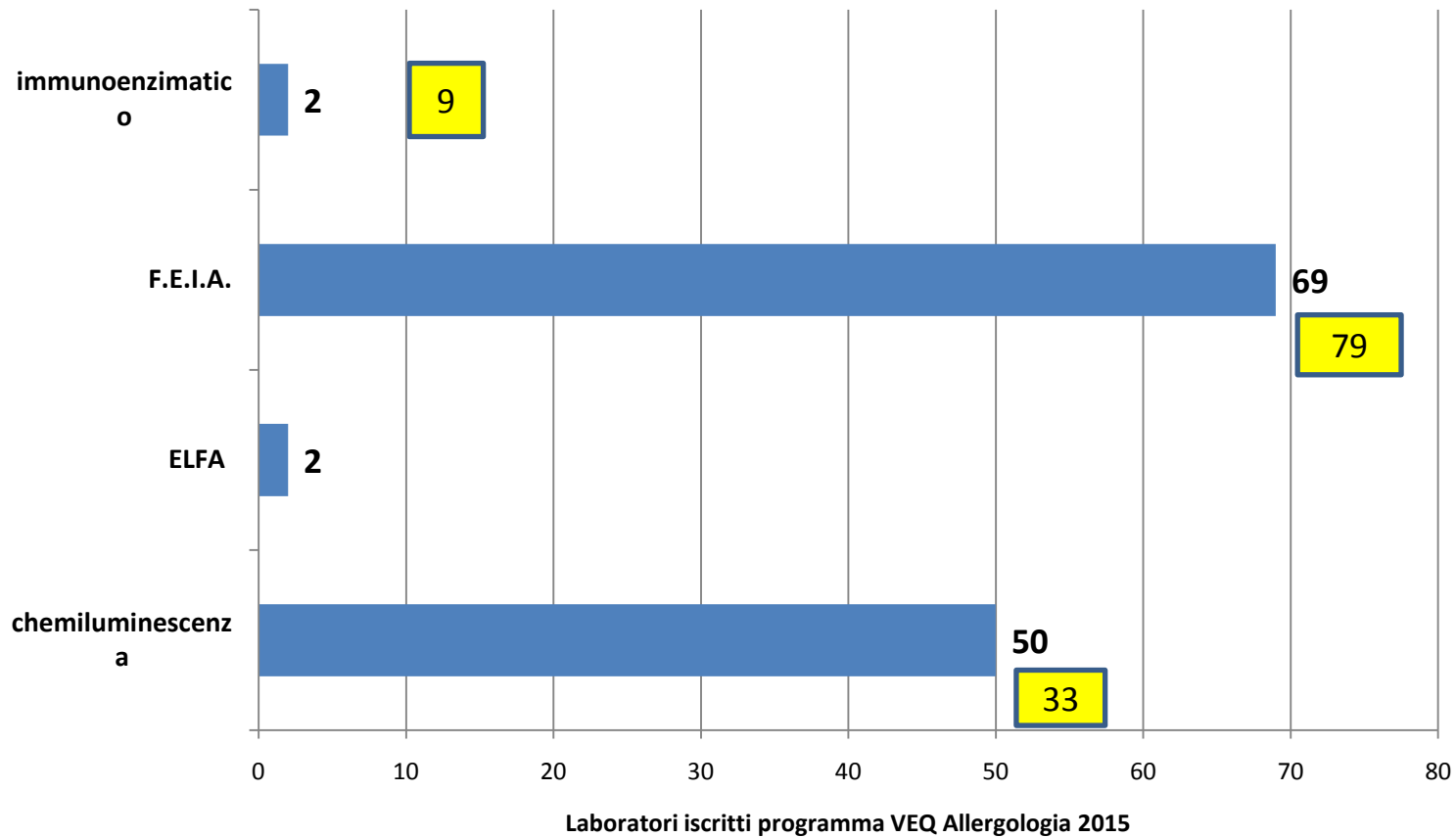
IgE totali metodi analitici

Anno 2014

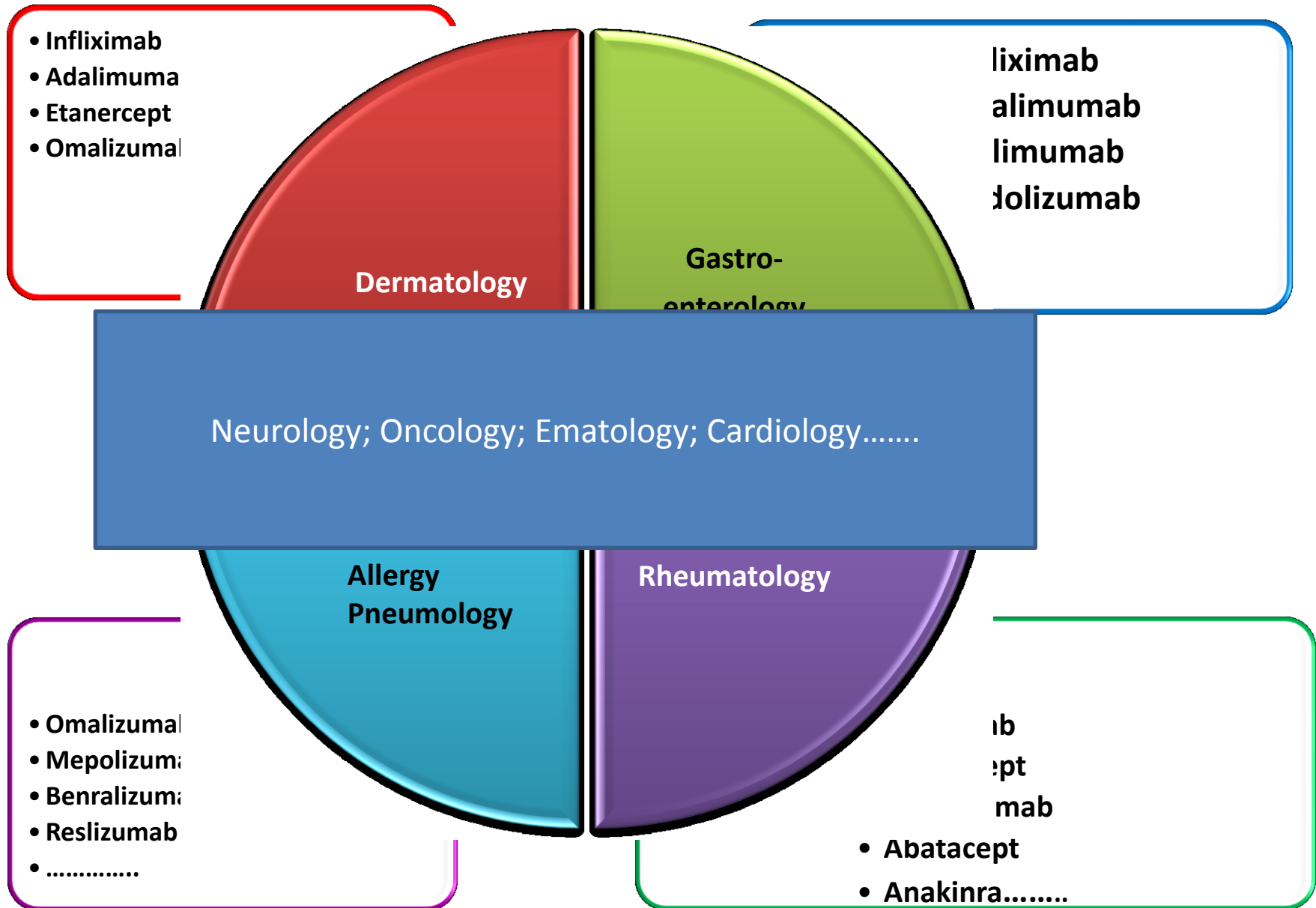


IgE Specifiche (2015) - metodi analitici

Anno 2014

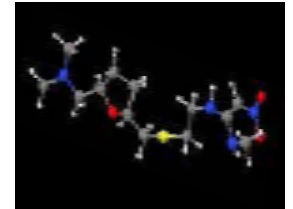


Immunogenicità dei farmaci biologici

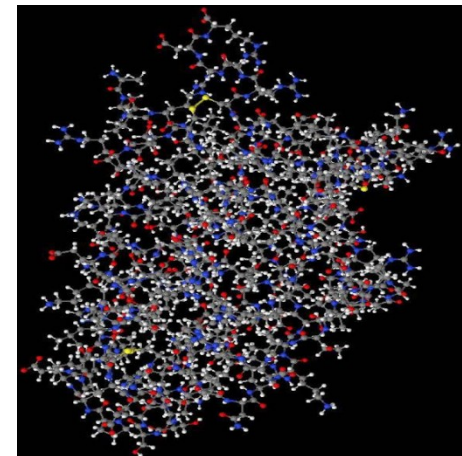


Farmaci biologici: perché sono immunogenici ?

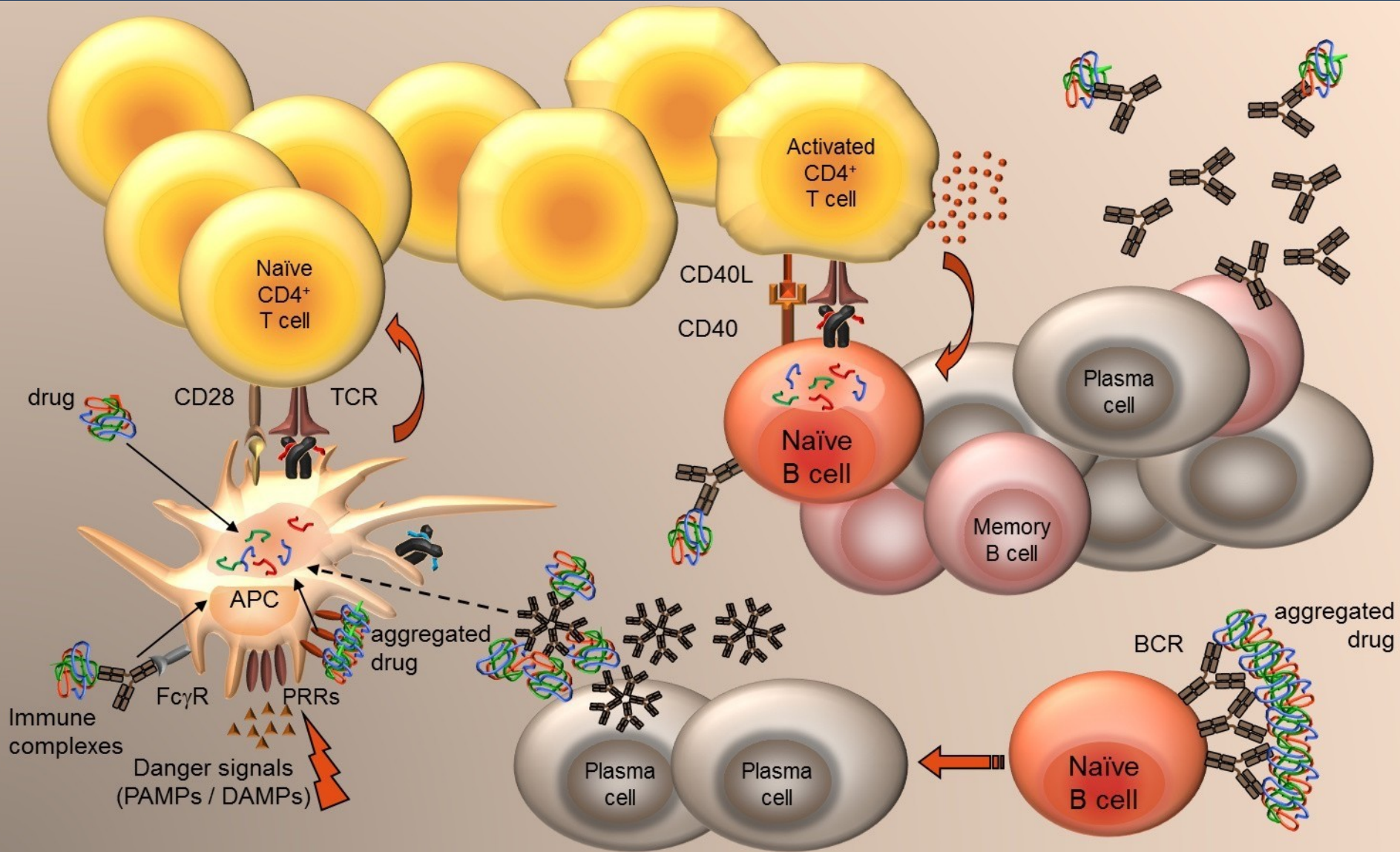
- Proteine grandi e complesse
- Presenza di xenoantigeni or process-related impurità
- Presenza di allotipi
- Presenza di idiotipo (mAbs)
- Neoantigeni nei siti di giunzione
- Siti di glicosilazione
- Formazione di aggregati



Tutti i farmaci biologici sono immunogenici

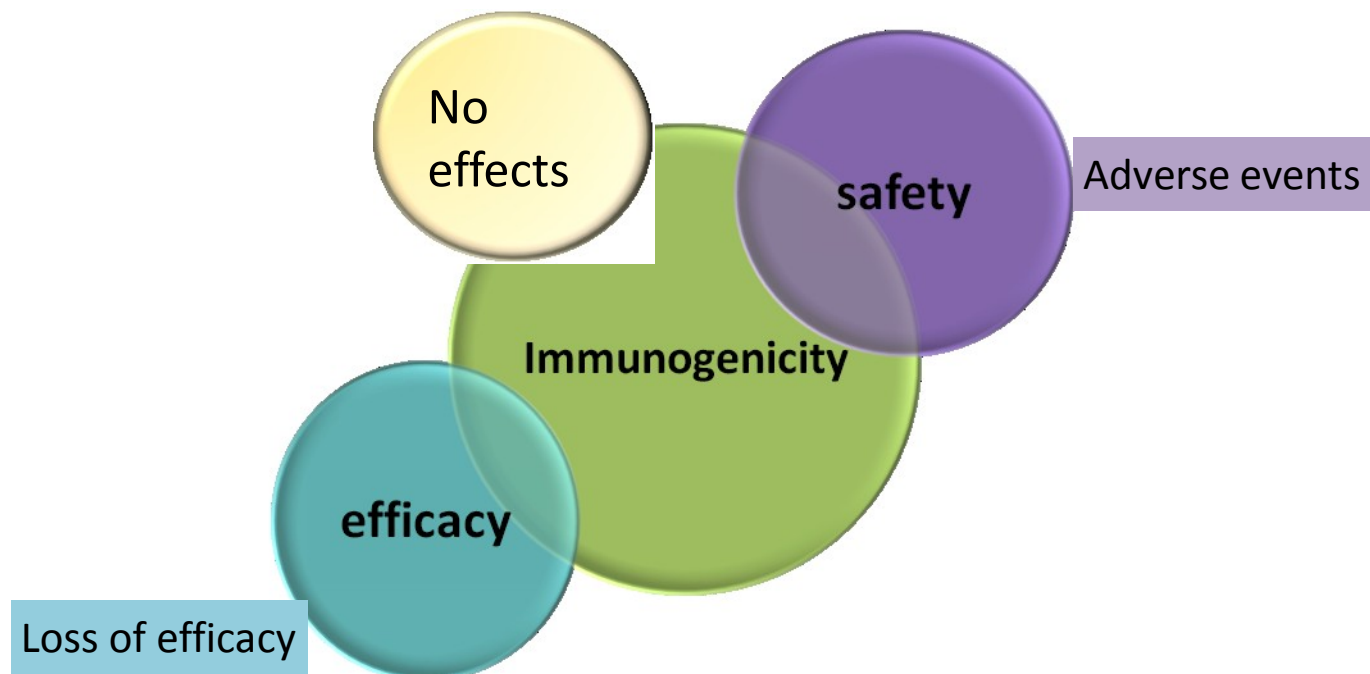


La risposta immune anti-farmaco biologico



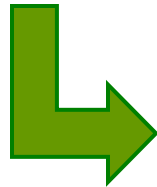
Perché siamo interessati all'immunogenicità?

L'immunogenicità porta allo sviluppo di anticorpi anti-farmaco (ADA) che possono avere due importanti conseguenze cliniche



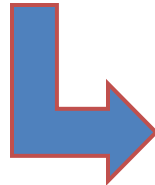
Immunogenicità come causa di perdita di efficacia dei farmaci biologici

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



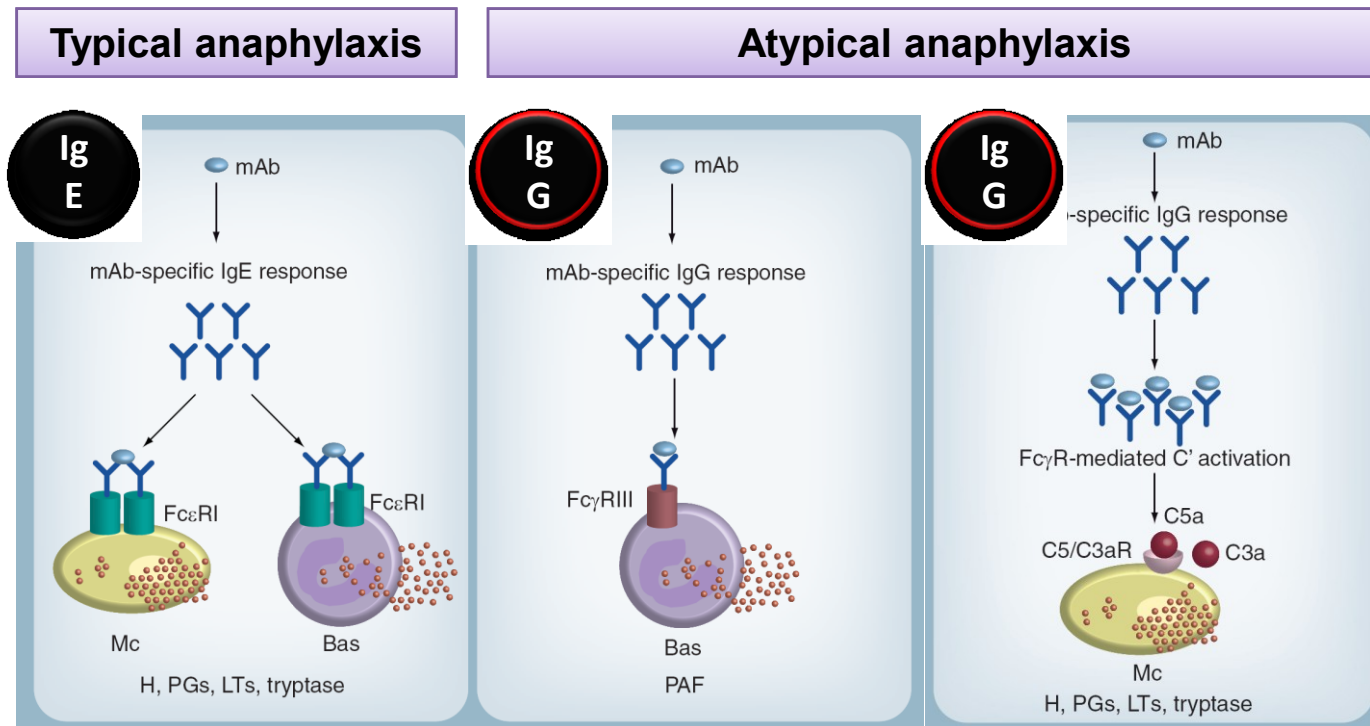
Farmaco biologicamente inattivo

2. Anticorpi cliranti: che incrementano la PK del farmaco



Farmaco metabolizzanto ppiù
velocemente

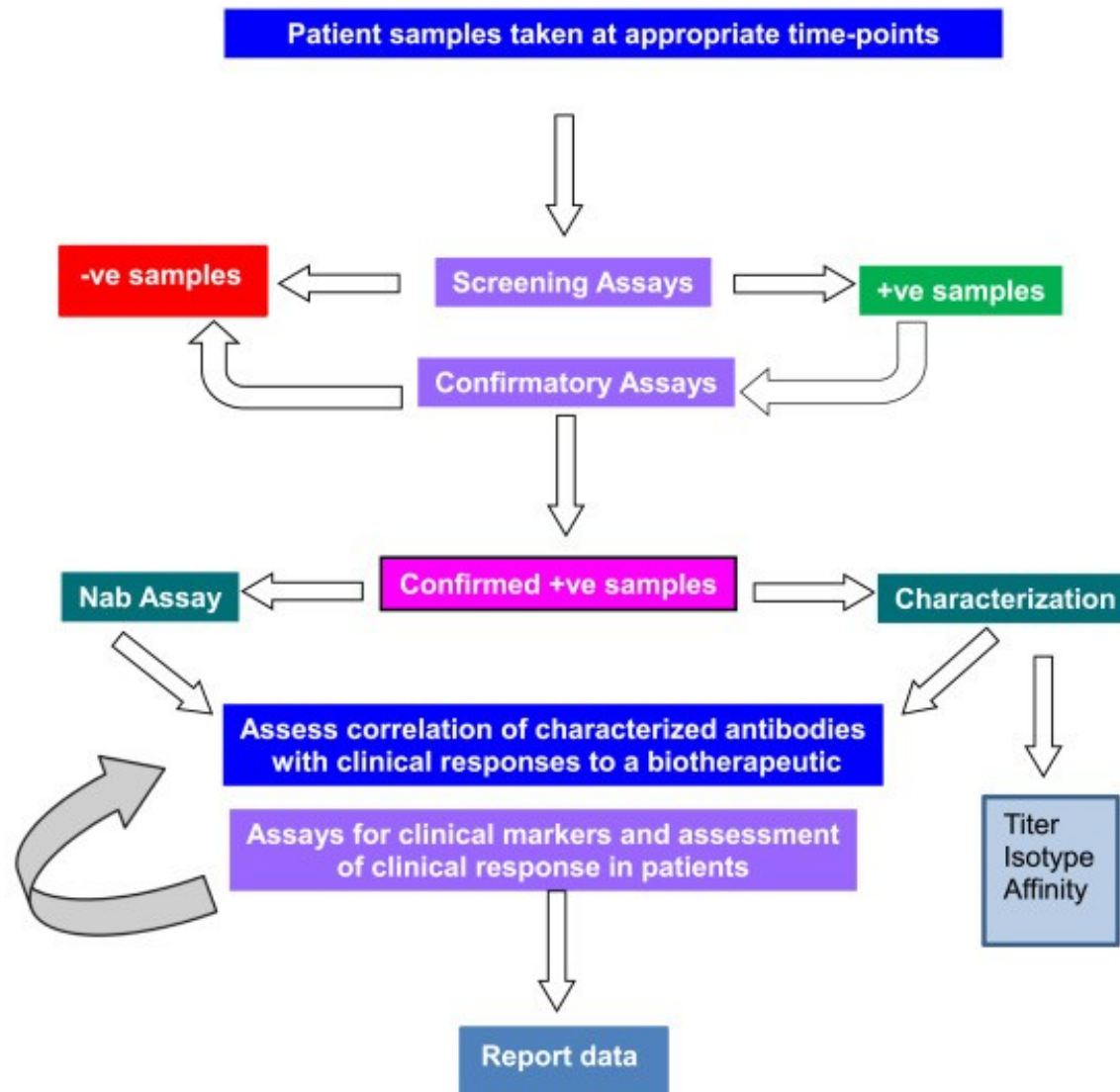
Anafilassi tipica ed atipica indotta da anticorpi anti-farmaco biologico



Maggi E, Vultaggio A, Matucci A
Exp Rev Clin Immunol 2011

Il ruolo del laboratorio

Strategia per la detezione degli anticorpi ADA



Detezione degli ADAs : metodi correnti

❑ Immunochemical methods

Binding assays (ELISAs, RIA, elettrochemiluminesce)

❑ Biophysical methods

Surface plasmon resonance

❑ Bioassays

Ciascun metodo ha i suoi vantaggi ed i suoi limiti

pros

Cons

Comparison of different techniques to monitor anti-drug antibodies

- Infliximab-treated patients
- BID patients (Crohn disease)
- Commercial ELISA, RIA, bridging ELISA home made



Performances of assays are comparable.

However, anti-IFX Ab titers show **systematic differences**, and in individual patients, **only the same assay should be used**.

Problems may arise when different assays are used to manage therapies in the same patient.

Testing for drug bioavailability and immunogenicity



Infliximab
Adalimumab
Etanercept
Certolizumab pegol
Golimumab
Rituximab
Tocilizumab
Bevacizumab
Trastuzumab
Ustekinumab



Abatacept
Natalizumab
Mepolizumab
Cetuximab
Belimumab

.....



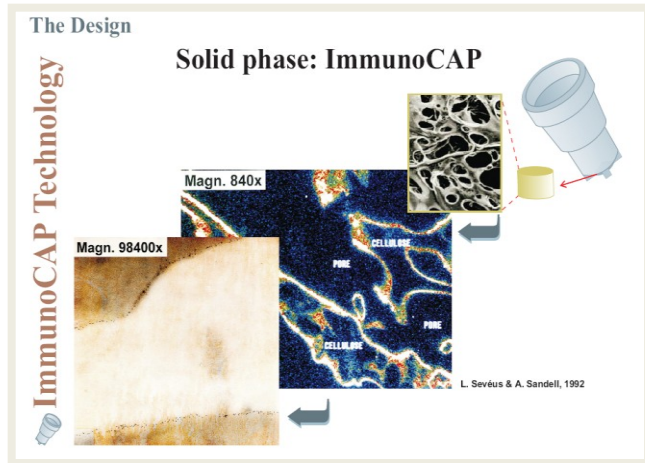
Home made
assay

IgE ADAs isotype: type of assay

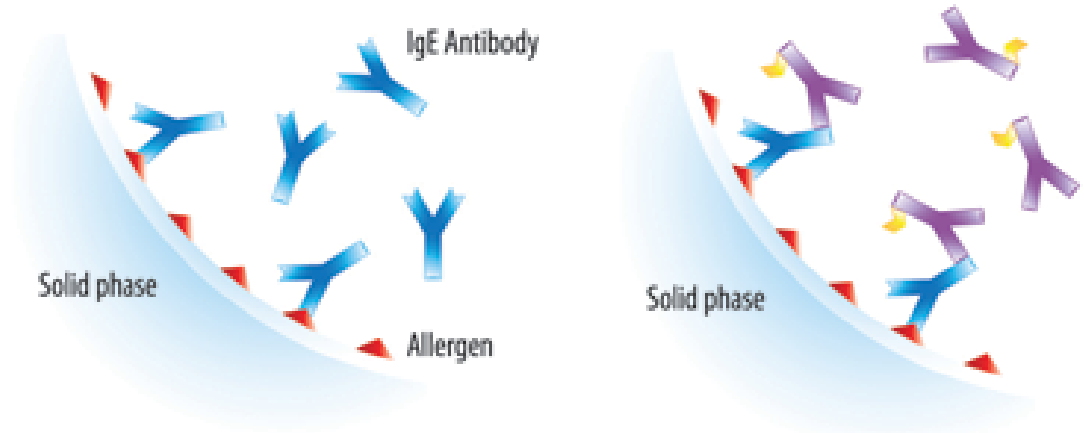
**IgE-mediated reactions have been described towards several BPs
by different assays**

Drug	In vitro	Ref
Muromonab	Yes, ELISA	Georgitis, 1991
Cetuximab	Yes, ImmunoCAP	Chung, 2008
Tocilizumab	Yes, ImmunoCAP	Stubenrauch, 2010
Basiliximab	Yes, ELISA	Baudouin , 2003
Natalizumab	Yes, ImmunoCAP	MunozCano, 2010
Infliximab	Yes, ImmunoCAP	Vultaggio, 2010, Matucci 2013
Rituximab	Yes, ImmunoCAP	Vultaggio, 2012

IgE ADAs isotype



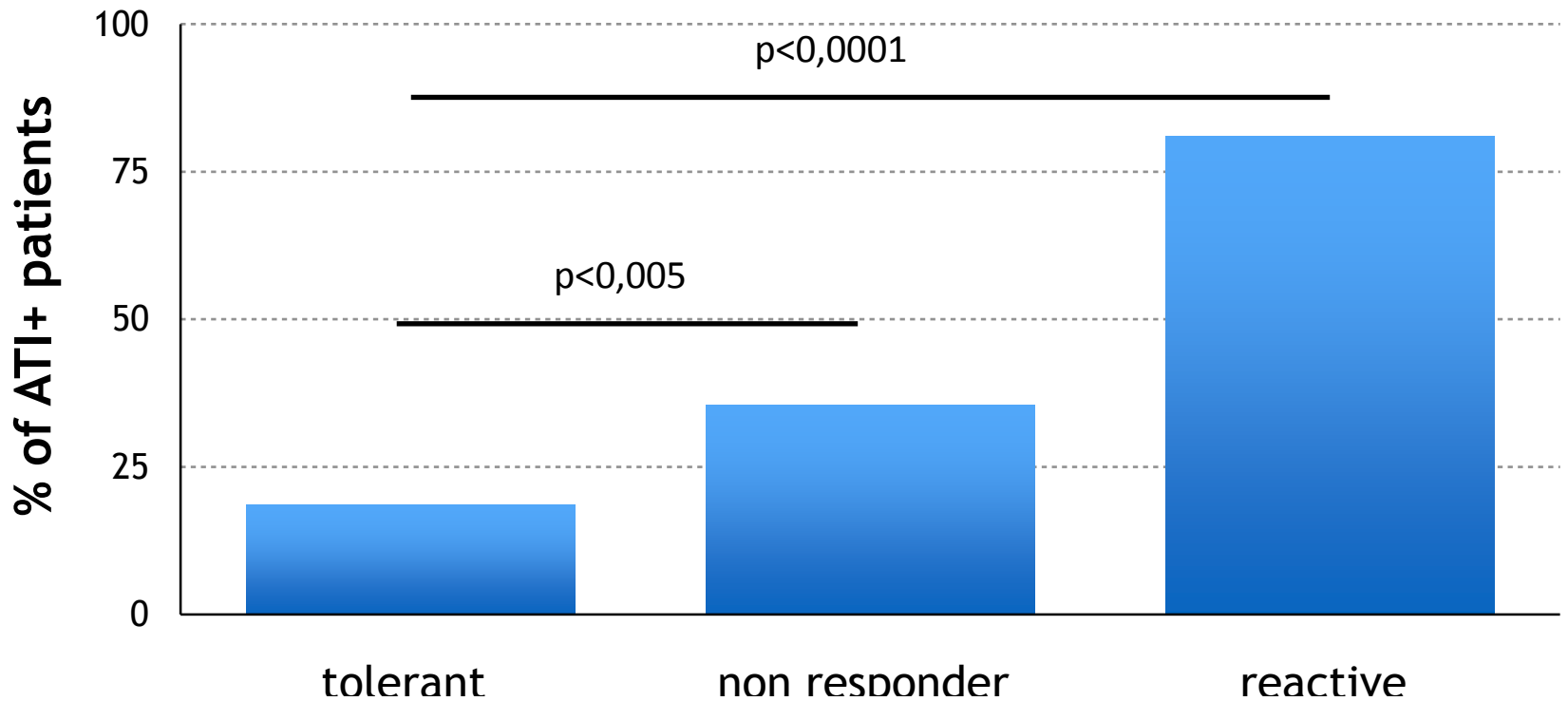
enzyme-labelled antibody against IgE



In the **ImmunoCAP system**, the allergen is covalently bound to a solid phase consisting of an activated hydrophilic polymer. The secondary IgE antibodies are bound to the enzyme β -galactosidase, which transforms added methylumbelliferyl- β -D-galactoside into a fluorescent product (4-methylumbelliferone). The fluorescence intensity depends on the concentration of the product and correlates with the IgE bound to the allergen.

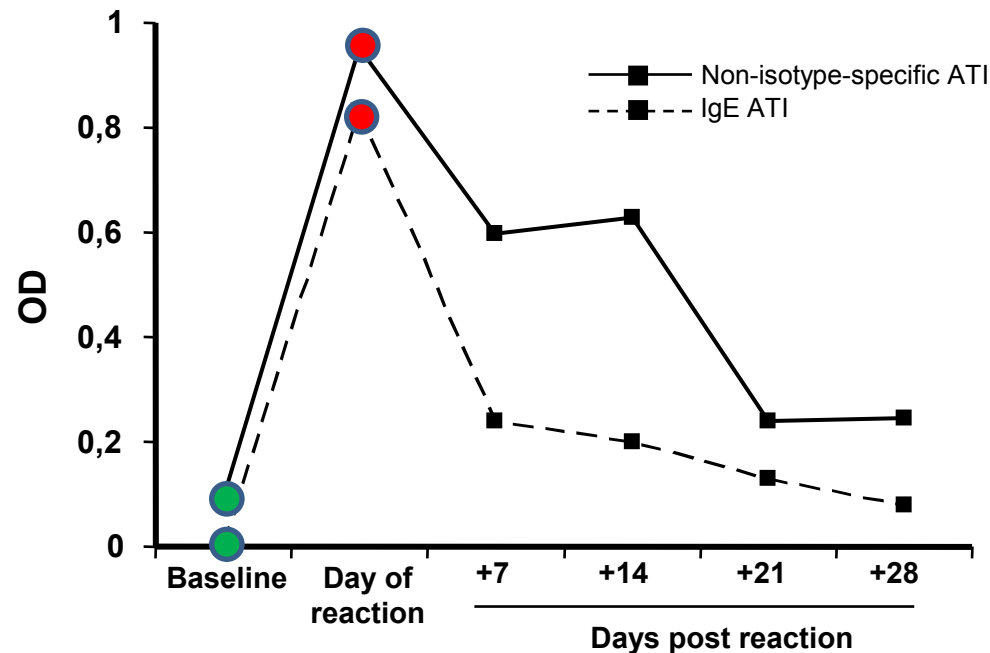
346 **Infliximab-treated** patients

Tolerant n=200
Non responder n=93
Reactive n=53



Benefits from immunogenicity evaluation

1) Predict the risk of hypersensitivity reactions?



**Hypersensitivity risk
can be detected prior to
clinical symptoms !!**



(A.Vultaggio, A.Matucci et al Allergy 2010)

Benefits from immunogenicity evaluation

2) Predict the clinical response?

Anti-drug antibodies

ORIGINAL ARTICLE

The relationship between infliximab concentrations, antibodies to infliximab and disease activity in Crohn's disease

Niels Vande Casteele,^{1,2,3} Reena Khanna,³ Barrett G Levesque,^{2,3} Larry Stitt,³ G Y Zou,³ Sharat Singh,⁴ Steve Lockton,⁴ Scott Hauenstein,⁴ Linda Ohrmund,⁴ Gordon R Greenberg,⁵ Paul J Rutgeerts,⁶ Ann Gils,¹ William J Sandborn,² Séverine Vermeire,⁶ Brian G Feagan³

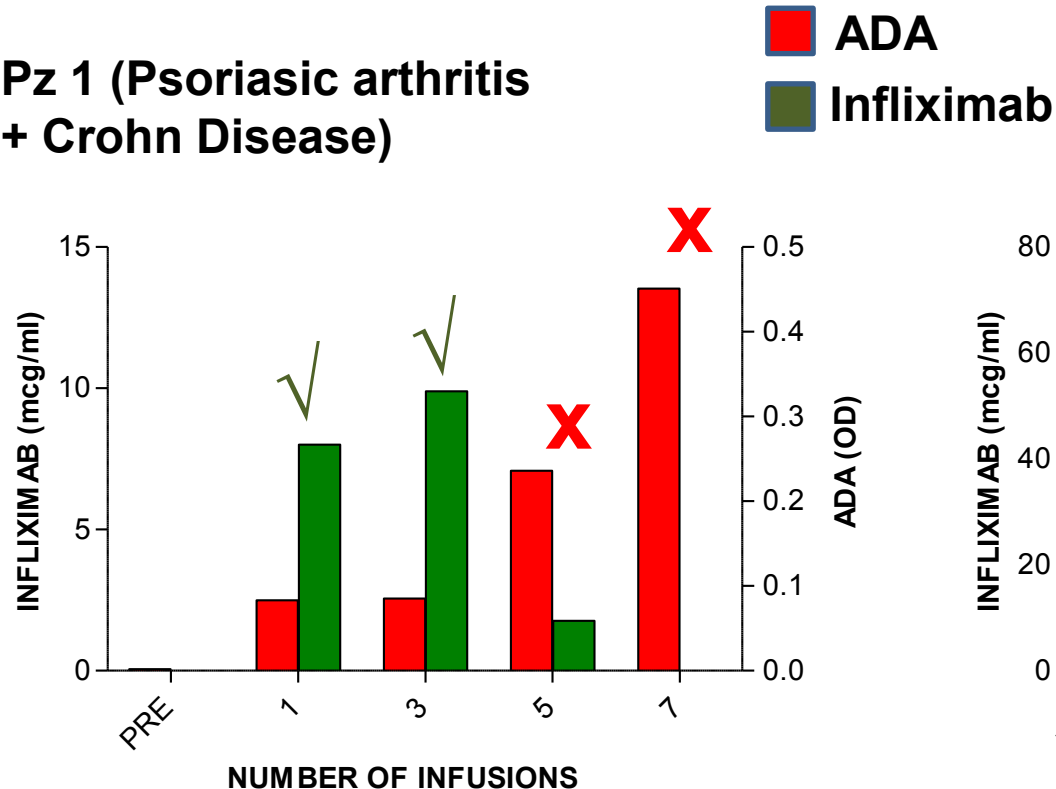
454 patients

ATI (anti-infliximab antibodies) presence in “current” sample is a independent predictor for the presence of C-Reactive Protein >5 mg/L (surrogate of disease activity) in a “future” sample ($p < 0.006$)

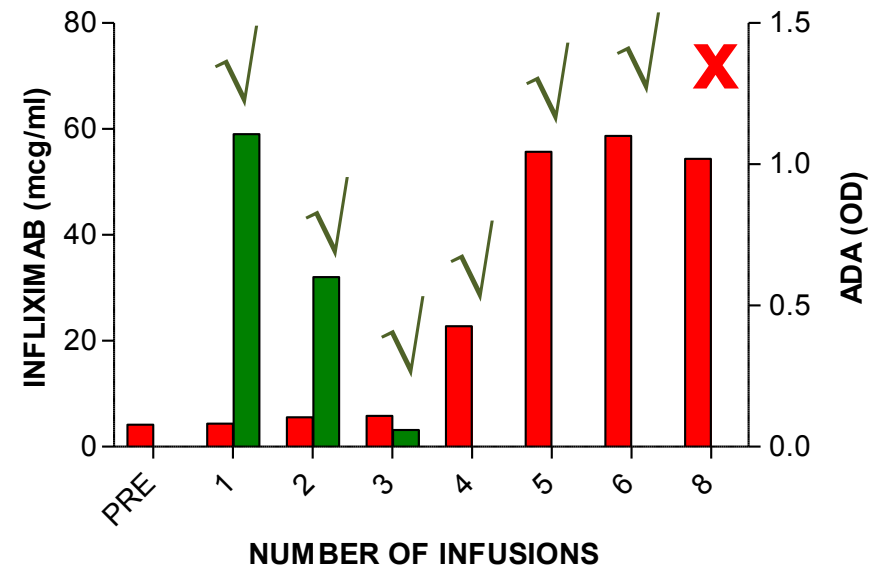
Δ time between “current” and “future” sample: 56 ± 14 days

Our experience in longitudinal evaluation of patients

Pz 1 (Psoriatic arthritis
+ Crohn Disease)



Pz 2 (Rheumatoid
Arthritis)



(Personal unpublished data)