I° CONVEGNO REGIONALE SIFO "MEETING DI PRIMAVERA" – "IL FARMACISTA CLINICO E I NUOVI MODELLI DI CURA"

Taormina, 11/12/13 maggio 2017

DAL FARMACO BIOLOGICO AI BIOSIMILARI

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Disclaimer

- Membro di Advisory Board sui biosimilari organizzati da Sandoz ed Hospira;

- In qualità responsabile scientifico di un un gruppo di ricerca di farmacoepidemiologia ho coordinato e sto coordinando studi osservazionali sui farmaci biologici e biosimilari finanziati da diverse aziende farmaceutiche (es. Amgen, Novartis, Daiichi Sankyo);

- Coordinatore scientifico del Master «Farmacovigilanza, Farmacoepidemiologia e Farmacoeconomia: valutazioni tramite real world data» che è stato finanziato da diverse aziende farmaceutiche produttrici di farmaci biologici e biosimilari.

Agenda

- In che contesto ci troviamo?
- Farmaci biologici e biosimilari: definizioni e principi di farmacologia
- Real world data sui biosimilari
- Farmaci biosimilari ed originator sono intercambiabili?

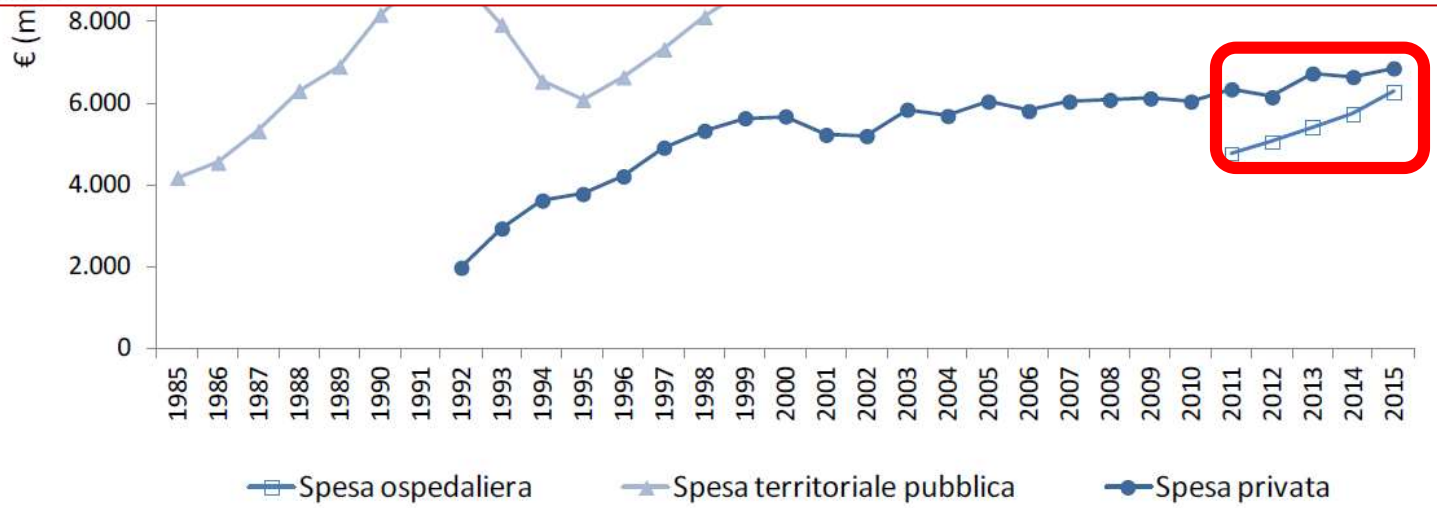
In che contesto ci troviamo?

Spesa farmaceutica negli anni 1985-2015

LA STAMPA 26/04/2016

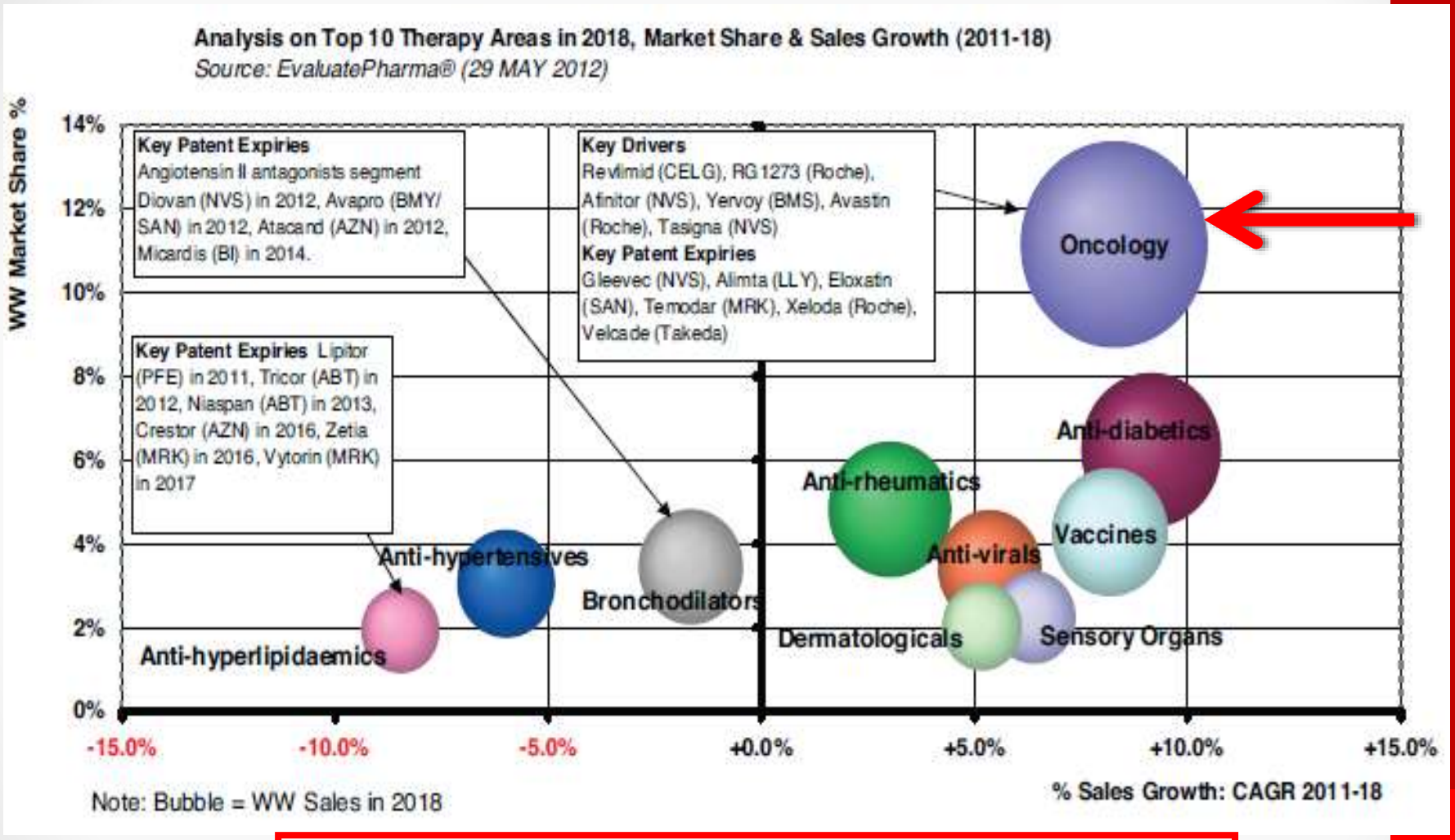
L'aspettativa di vita degli Italiani? In calo per la prima volta nella storia

Dal rapporto Osservasalute nel 2015 il trend per gli uomini è stato 80,1 anni e 84,7 per le donne



OsMed 2015

Evoluzione della Terapia Farmacologica: 2011 - 2018



L'innovazione offre nuove opzioni terapeutiche ma ad alto impatto economico

Fonte: Farmindustria

Marketed and under development drugs for inflammatory diseases

1) Global immunosuppressive agents, excluding multiple sclerosis and oncology Source: EvaluatePharma
2) Other MOA includes IL-6, B-cell, T-cell

L'innovazione bisogna meritarsela!

A Delicate Balance — Pharmaceutical Innovation and Access

William W. Chin, M.D.

N ENGL J MED 373;19 NEJM.ORG NOVEMBER 5, 2015

- Our system recognizes the considerable challenges and expense of the research and development process and the need to reward innovation, and it balances these needs against access;
- Payers demand demonstration of value and drive patients to the lowest cost options using aggressive cost containment strategies;
- US makes more efficient use of generics than other countries: nearly 90% of all U.S. prescriptions are filled with generics that are sold at a fraction of the price of the original brand-name medication, helping ensure long-term affordability;
- And the new biosimilars pathway is expected to deliver additional cost savings.

Impact of generics on drug expenditure and volume of use in Italy (year 2015)

ATC I livello	Spesa (Ass. convenzionata e strutture sanitarie pubbliche)		Consumo -DDD (Ass. convenzionata e strutture sanitarie pubbliche)	
	% Brevetto scaduto per categoria terapeutica	% Generico per area terapeutica	% Brevetto scaduto per categoria terapeutica	% Generico per area terapeutica
A	46,2%	16,3%	70,6%	23,9%
B	7,3%	2,0%	61,0%	10,4%
C	56,0%	14,4%	83,2%	28,5%
D	23,5%	4,9%	8,8%	1,5%
G	30,3%	8,9%	61,1%	20,4%
H	15,3%	0,8%	69,5%	2,6%
J	20,4%	5,1%	77,0%	20,9%
L	3,9%	0,9%	43,1%	21,8%
M	41,3%	9,5%	67,1%	21,9%
N	15,8%	5,1%	59,2%	27,1%
P	5,5%	1,1%	7,4%	3,6%
R	11,8%	1,9%	34,0%	7,1%
S	12,9%	2,1%	38,7%	10,4%
V	1,9%	0,3%	7,9%	1,2%

OsMed 2015

Top 30 molecules accounting for drug expenditure in Italian hospitals

	Principio attivo	ATC I	Classe	Spesa	Inc%	Cum%
1	Sofosbuvir	J	A	1.258.960.429	19,4%	19,4%
2	Fattore VIII	B	A	200.578.540	3,1%	22,5%
3	Adalimumab	L	H	186.071.453	2,9%	25,4%
4	Daclatasvir	J	A	159.832.738	2,5%	27,8%
5	Ritonavir/Ombitasvir/ Paritaprevir	J	A	150.592.760	2,3%	30,2%
6	Etanercept	L	H	143.492.783	2,2%	32,4%
7	Lenalidomide	L	H	135.542.864	2,1%	34,5%
8	Imatinib Mesilato	L	A	124.984.810	1,9%	36,4%
9	Fingolimod	L	A	82.248.058	1,3%	37,7%
10	Emtricitabina/Tenofovir Disoproxil	J	H	74.008.370	1,1%	38,8%
11	Abiraterone Acetato	L	H	72.581.700	1,1%	39,9%
12	Interferone Beta 1A Ricombinante	L	A/C	70.481.908	1,1%	41,0%
13	Rivaroxaban	B	A	69.693.916	1,1%	42,1%
14	Insulina Glargine	A	A	67.961.702	1,0%	43,1%
15	Bosentan	C	A/H	62.906.439	1,0%	44,1%
16	Somatropina	H	A	62.722.046	1,0%	45,1%
17	Entecavir	J	A/C	58.921.801	0,9%	46,0%
18	Apixaban	B	A	58.027.262	0,9%	46,9%
19	Emtricitabina/Tenofovir Disoproxil/Rilpivirina	J	A/H/C	55.033.937	0,8%	47,7%
20	Everolimus	L	A/H/C	54.976.737	0,8%	48,6%
21	Dimetilfumarato	N	A	54.195.830	0,8%	49,4%
22	Dabigatran Etexilato	B	A	53.089.524	0,8%	50,2%
23	Golimumab	L	H	50.012.910	0,8%	51,0%
24	Darunavir	J	H	49.956.815	0,8%	51,8%
25	Darbepoetina Alfa	B	A	49.912.462	0,8%	52,5%
26	Epoetina Alfa	B	A/H	49.017.217	0,8%	53,3%
27	Abacavir Solfato/Lamivudina	J	H	47.973.205	0,7%	54,0%
28	Deferasirox	V	A	46.398.307	0,7%	54,7%
29	Nilotinib	L	H	45.981.111	0,7%	55,4%
30	Dasatinib	L	H	45.630.050	0,7%	56,2%
	Totale Italia			**6.485.511.858**	**100,0%**	

OsMed 2016 (Jan-Sep)

21 Biosimilars approved by EMA as of Sept. 2016

INN	Biosimilar	Developing company	Approved
Somatropin	Omnitrope®	Sandoz	Apr-06
Epoetin α	Binocrit® / Epoetin Alfa Hexal®	Sandoz (Hexal)	Aug-07
	Abseamed®	Medice	Aug-07
Epoetin ζ	Retacrit®	Hospira	Dec-07
	Silapo®	Stada	Dec-07
Filgrastim	Ratiograstim®	Ratiopharm	Sep-08
	Tevagrastim®	Teva	Sep-08
	Biograstim®	CT Arzneimittel	Sep-08
	Zarzio® / Filgrastim Hexal ®	Sandoz (Hexal)	Feb-09
	Nivestim™	Hospira	Jun-10
	Grastofil®	Apotex	Oct-13
	Accofil®	Accord	Sep-14
Infliximab	Inflectra®	Hospira	Sep-13
	Remsima™	Celltrion	Sep-13
	Flixabi®	Samsung Bioepis	May-16
Follitropin α	Ovaleap®	Teva	Sep-13
	Bemfola®	Finox Biotech	Mar-14
Insulin glargine	Abasaglar® (formerly Abasria)	Eli Lilly / Boehringer Ingelheim	Sep-14
Etanercept	Benepali®	Samsung Bioepis	Jan-16

EMA website

The next wave of biosimilars include trastuzumab, rituximab, adalimumab and bevacizumab in Europe

Europe: Recent biosimilar filings

Originator Name (molecule name)	Therapeutic area	Total pending EMA applications	Originator protection expiry	European revenue 2016 (Bn €)
Enbrel (etanercept)	Autoimmune	+ 1	Aug-15	€2.0 Bn
Lantus (insulin glargine)	Diabetes	+ 1	May-15	€1.1 Bn
Herceptin (trastuzumab)	Oncology	3	Jul-14	€1.8 Bn
Mabthera (rituximab)	Oncology	+ 2	Feb-13	€1.7 Bn
Avastin (Bevacizumab)	Oncology	2	Jan-22	€1.8 Bn
Humira (adalimumab)	Autoimmune	4	Apr-18	€3.4 Bn
Neulasta (pegfilgrastim)	Oncology	3	Aug-17	€0.5Bn

Courtesy of P. Troein - IMSQuintiles

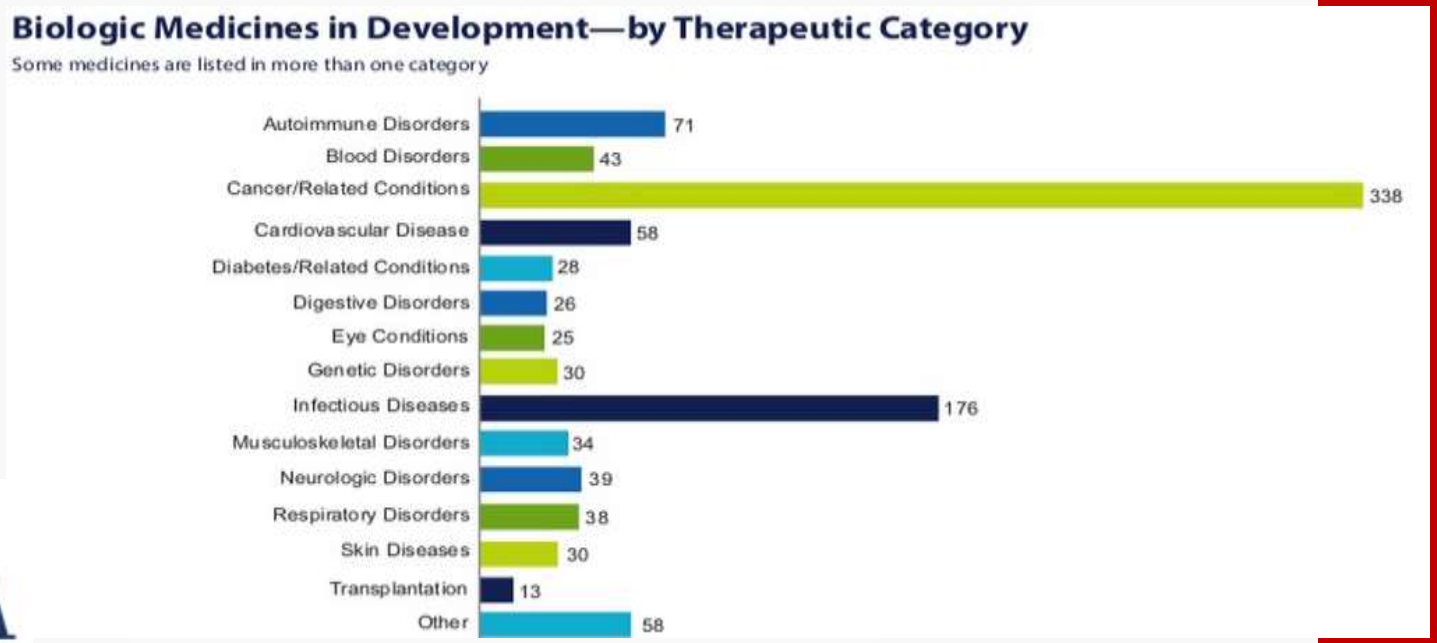
Farmaci biologici e biosimilari

Definizioni e principi di farmacologia

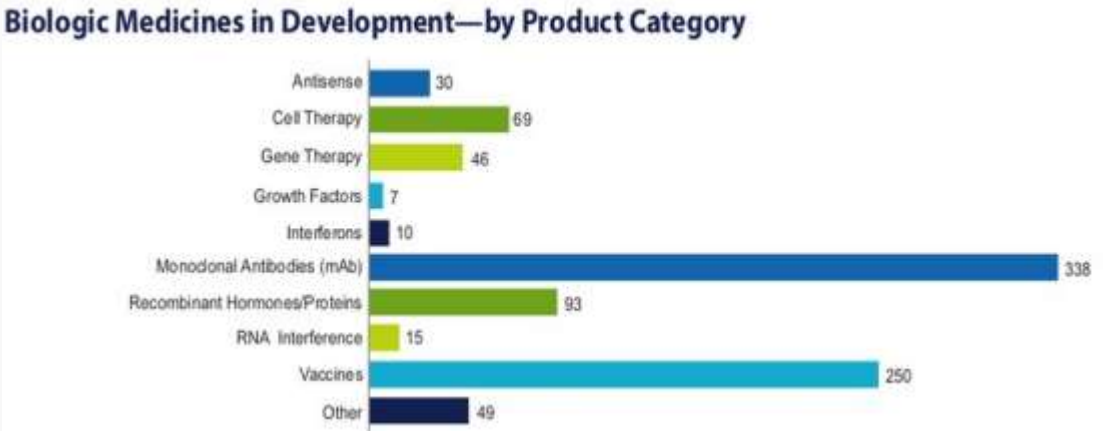
Farmaci biologici

Biologici: prodotti o derivati da organismi viventi

Biotecnologia: tecnologia per la manipolazione degli organismi viventi finalizzata alla produzione di specifiche proteine, quali ormoni ed anticorpi monoclonali



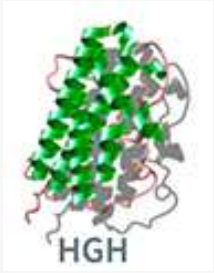
PhRMA
RESEARCH • PROGRESS • HOPE

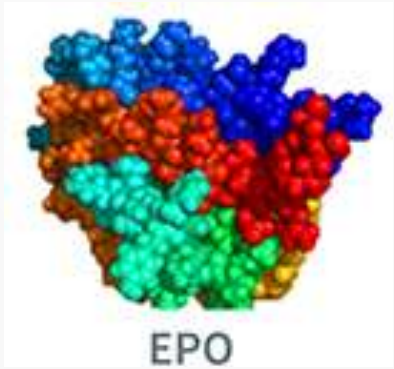


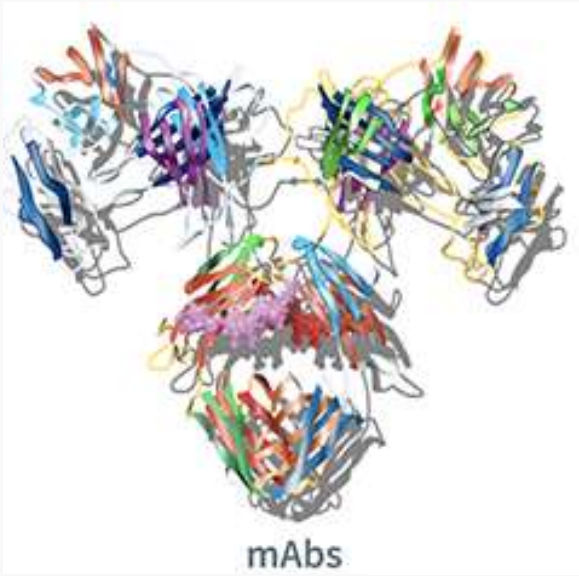
Simple and Complex Biologics

- Simple biologics can be synthetized or made from living cells

- Complex biologics are produced in living cells







Current EMA definition of biosimilar

*"A biosimilar is a **biological medicinal product that contains a version of the active substance of an already authorised original biological medicinal product** (reference medicinal product) in the EEA. Similarity to the reference medicinal product in terms of quality characteristics, biological activity, safety and efficacy based on a comprehensive comparability exercise needs to be established"*

Abbreviation: EEA: European economic area

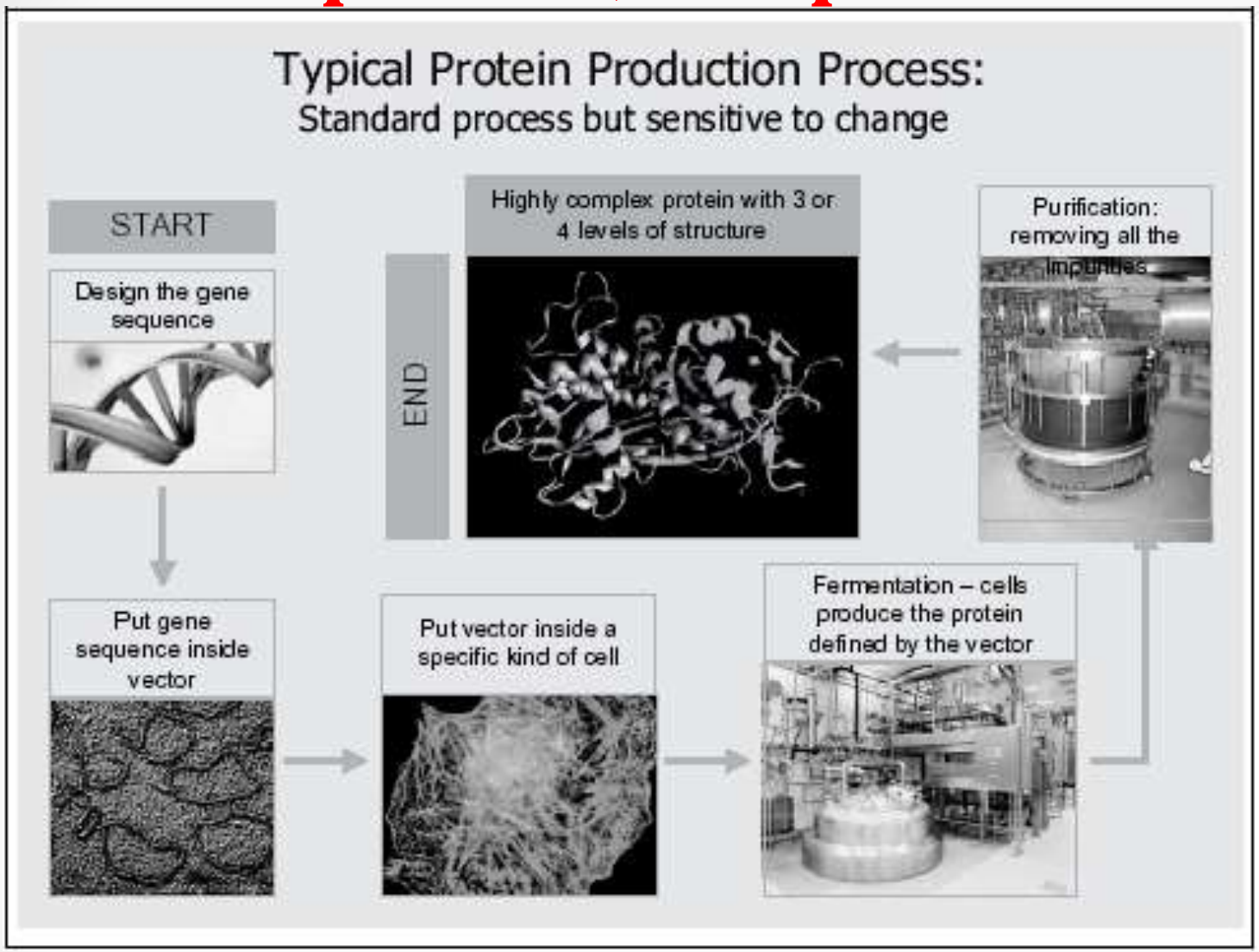
1. EMA. http://www.ema.europa.eu/../WC500176768.pdf [Accessed May 2015].

Higher development costs for biologics & biosimilars

	Generic	Biosimilar	Original Biologic
Development Costs	$1-5 Mil	$100-200 Mil	Up to $800 Mil
Development Time	3-5 years	5-8 years	Up to 12 years
Discount over reference product	80-90%	~ 20-30% or more	–

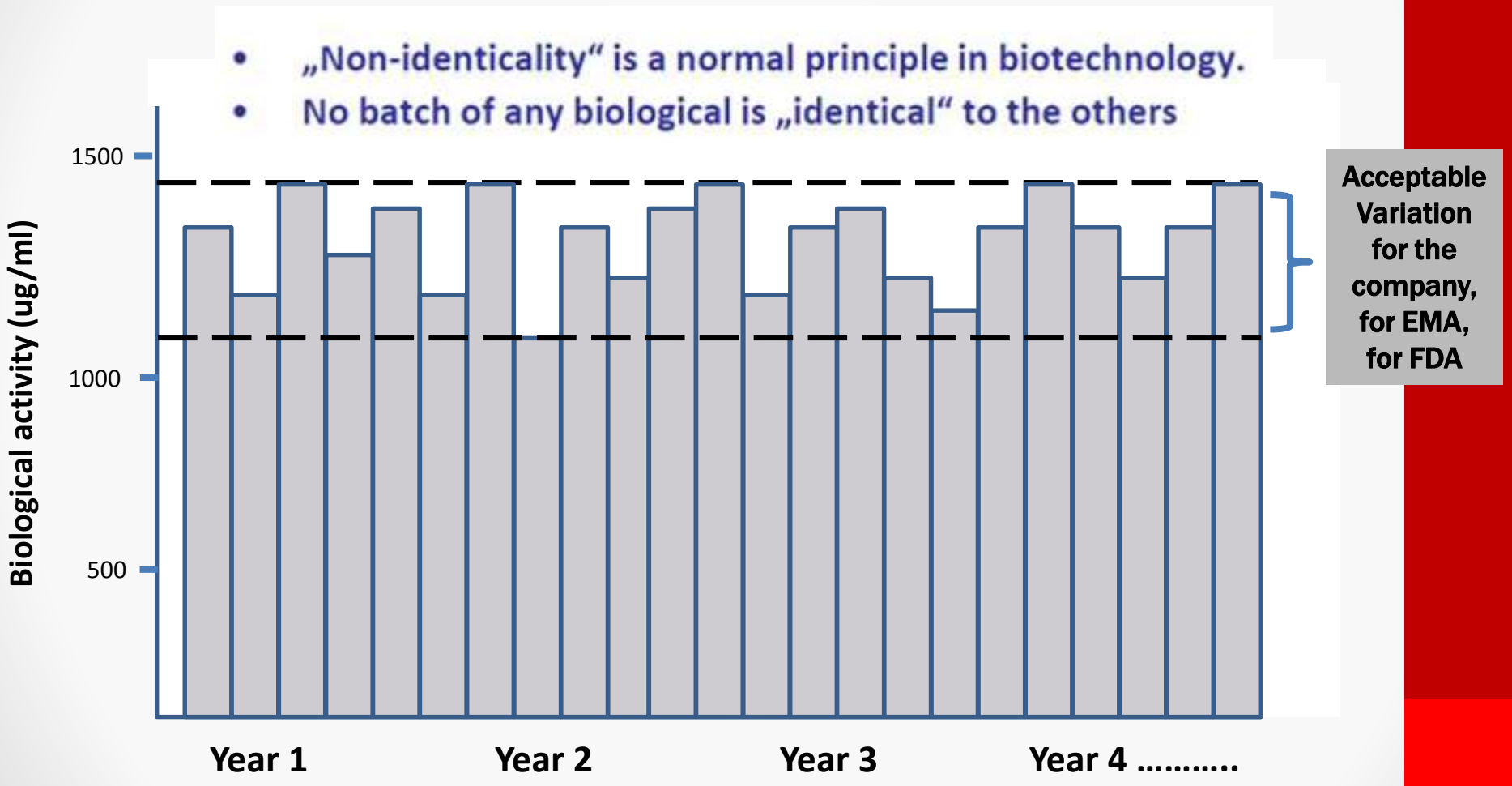
Source: Deloitte Winning with Biosimilars 2015

“One process, one product”



Quanto frequenti e clinicamente rilevanti i cambiamenti nel processo di produzione?

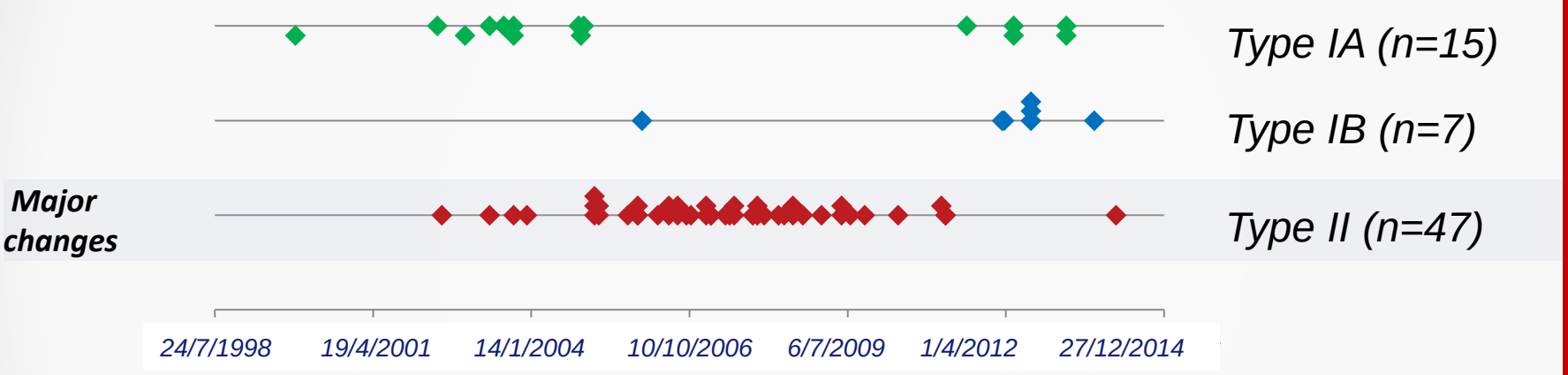
Biologicals are similar but not identical



Disclaimer: Hypothetic mAb production

Post-approval changes of Remicade (infliximab) production

Manufacturing changes are a normal process in all biologics!



Comparability exercises validated that these major (Type II) manufacturing changes did not impact the quality, safety and efficacy of the drug.

Type IA Variation

- Minimal or no impact on the quality, safety, or efficacy of the medicinal product concerned
- Notification procedure

Type IB Variation

- Variation which is neither Type IA nor Type II
- Notification procedure

Type II Variation

- A significant impact on the quality, safety, or efficacy of a medicinal product
- Prior approval procedure

1. EMA. http://www.ema.europa.eu/../WC500050890.pdf. [Accessed May 2015].

COMPARABILITY EXERCISE

Comparazione qualità

- Caratterizzazione analitica completa
- Studi di legame recettoriali
- Test biologici

Comparazione non-clinica

- Studi in vitro ed in vivo

Comparazione clinica

- Farmacocinetica (assorbimento, clearance, emivita)
- Farmacodinamica (marker clinicamente rilevanti, curve dose-risposta)
- Efficacia
- Immunogenicità
- Sicurezza

AIFA. Position Paper sui Farmaci Biosimilari (2013). Disponibile online: http://www.agenziafarmaco.gov.it/sites/default/files/AIFA_POSITION_PAPER_FARMACI_BIOSIMILARI.pdf;
AIFA. Approfondimento su: farmaci biotecnologici e biosimilari. BIF XV N.3 2008; 128-9

Biosimilars “inverted pyramid”

Originator Biologic

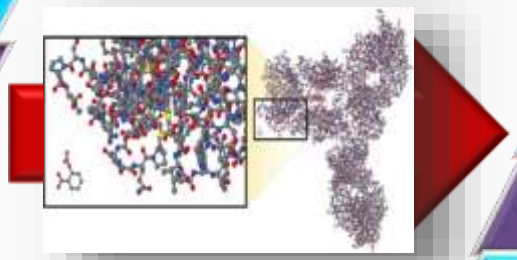
Phase III Clinical Studies

Phase II Clinical Studies

Phase I Clinical Studies

Nonclinical Studies

Molecule Character-ization



Biosimilar

+ Scientific Justification

Clinical Studies

PK / PD

Nonclinical Studies

Functional (biological) Characterization

Physicochemical Characterization

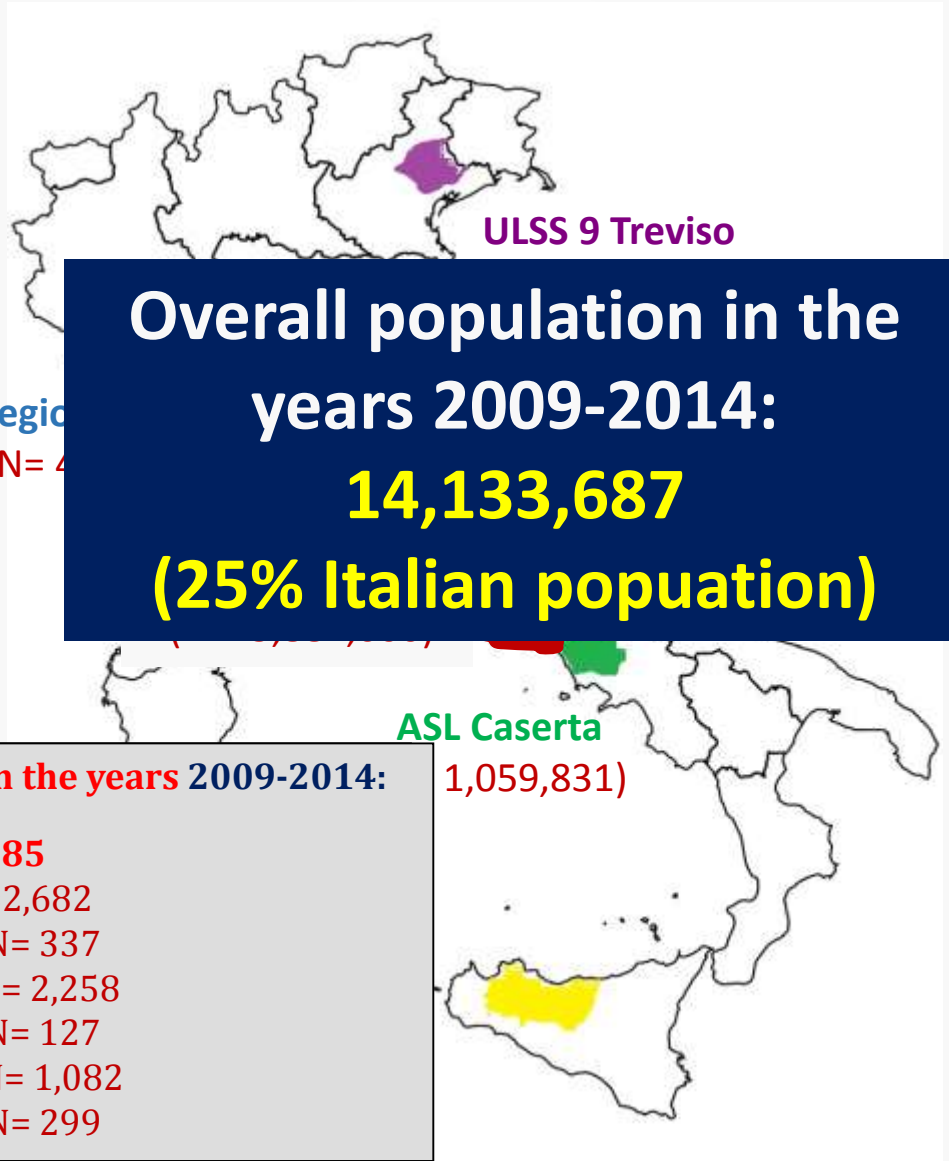
“Higher regulatory ”emphasis”

“Lower regulatory emphasis”

Size of pyramid = “quantity” of effort

Real world data sui biosimilari

Assessment of short and long term risk-benefit profile of biologics/biosimilars through healthcare database network in Italy



Overall population in the years 2009-2014:

14,133,687

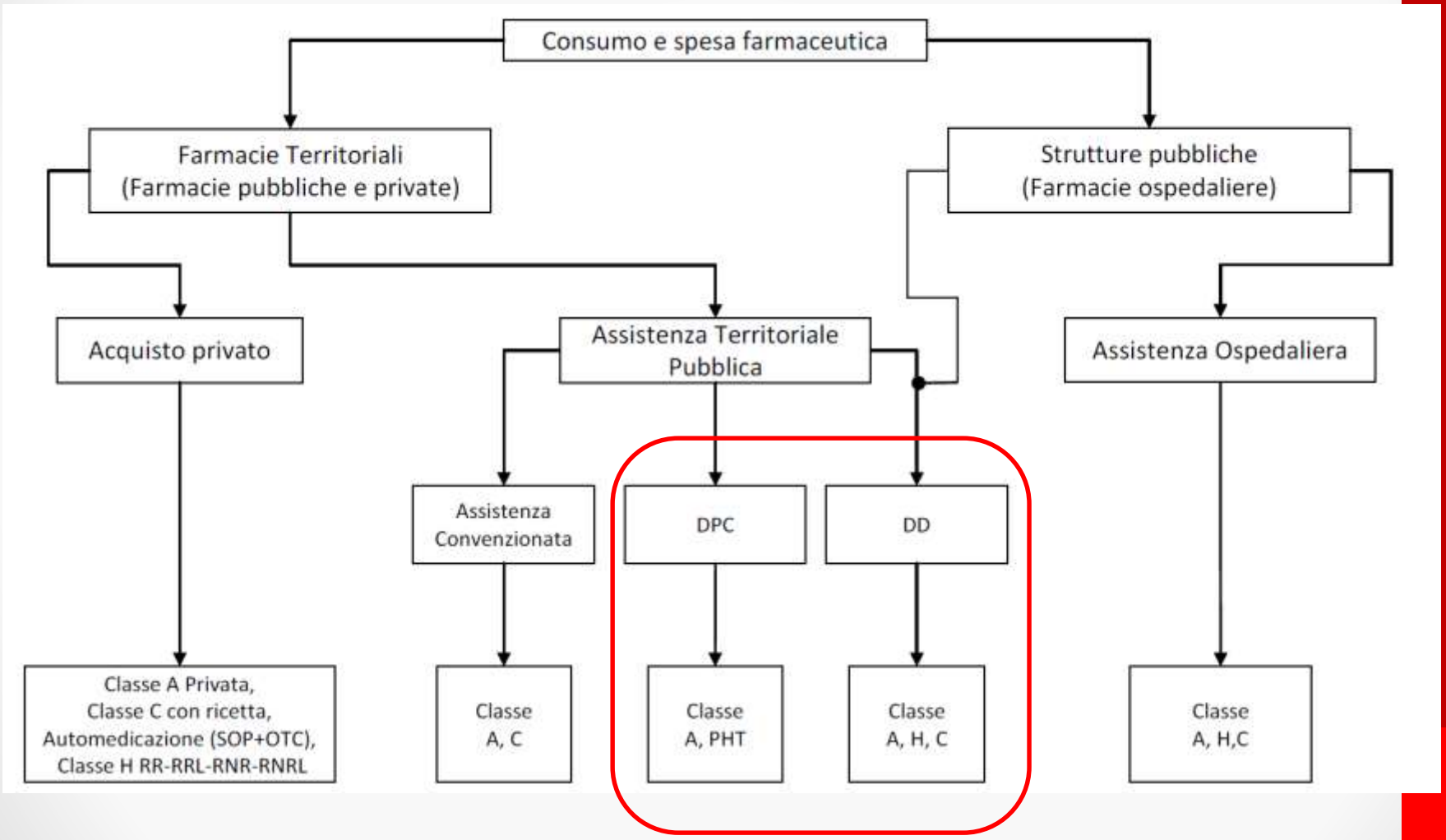
(25% Italian popuation)

N. users of somatotropin in the years 2009-2014:

N= 6,785

Lazio: N=2,682
Caserta: N= 337
Toscana: N= 2,258
Treviso: N= 127
Palermo: N= 1,082
Umbria: N= 299

Traceability of biologicals and biosimilars in Italy



OsMed 2015

D.A. n. 540/14

Misure volte a promuovere l'utilizzo dei farmaci Originatori o Biosimilari a minor costo di terapia

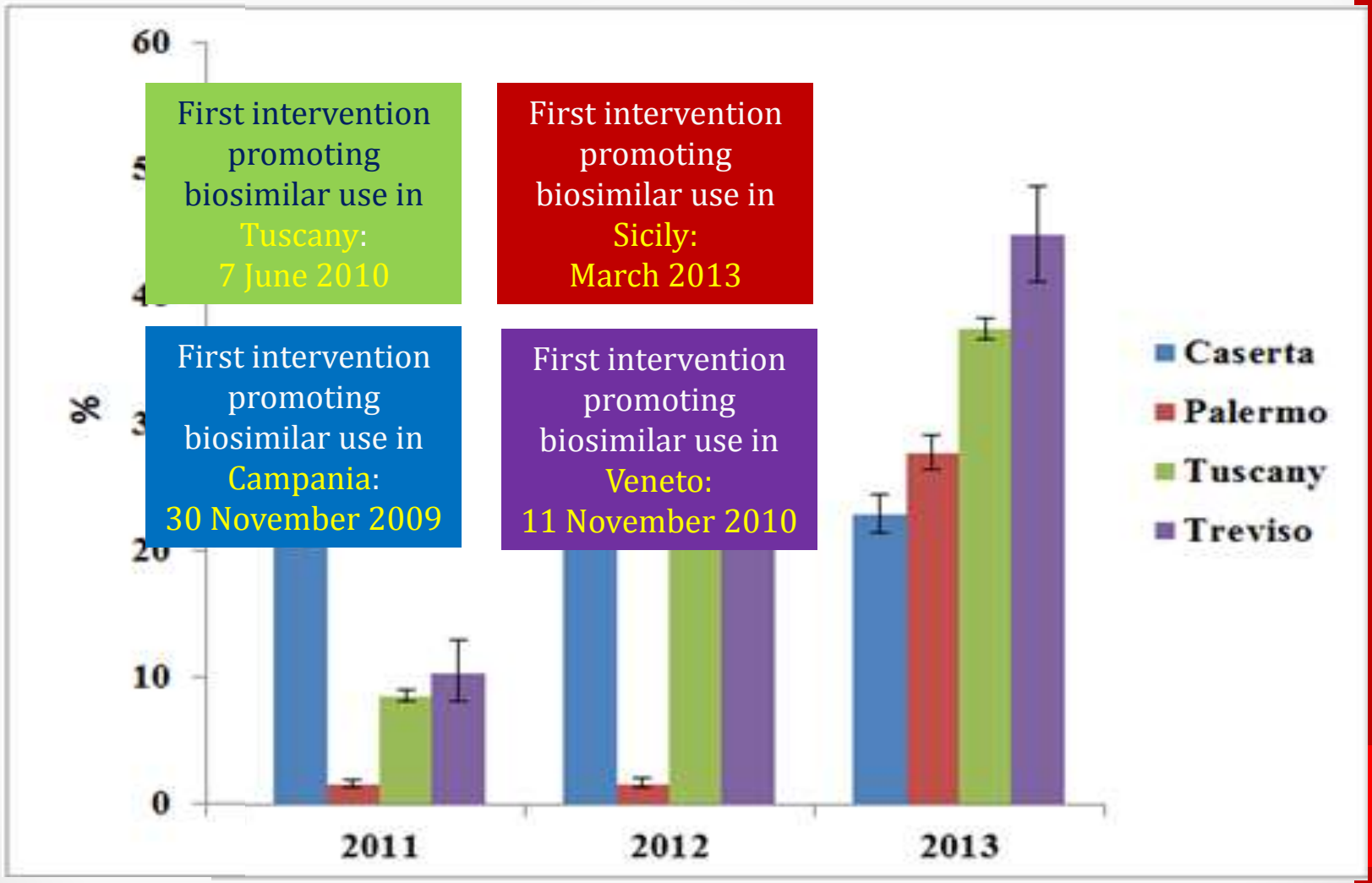
- Il farmaco di riferimento o biosimilare, a minor costo, deve essere utilizzato come prima scelta nel paziente *naive*, cioè mai trattato o esposto a nuovo trattamento dopo adeguato *washout*, salvo diverso giudizio clinico;

- in caso di documentata inefficacia terapeutica e/o intolleranza e/o effetti collaterali, va garantito il ricorso ad altro farmaco biosimilare o di riferimento;

- Qualora il medico non ritenga di poter utilizzare il biologico di riferimento o biosimilare a minor costo è tenuto, contestualmente alla prescrizione, a produrre le motivazioni della scelta;

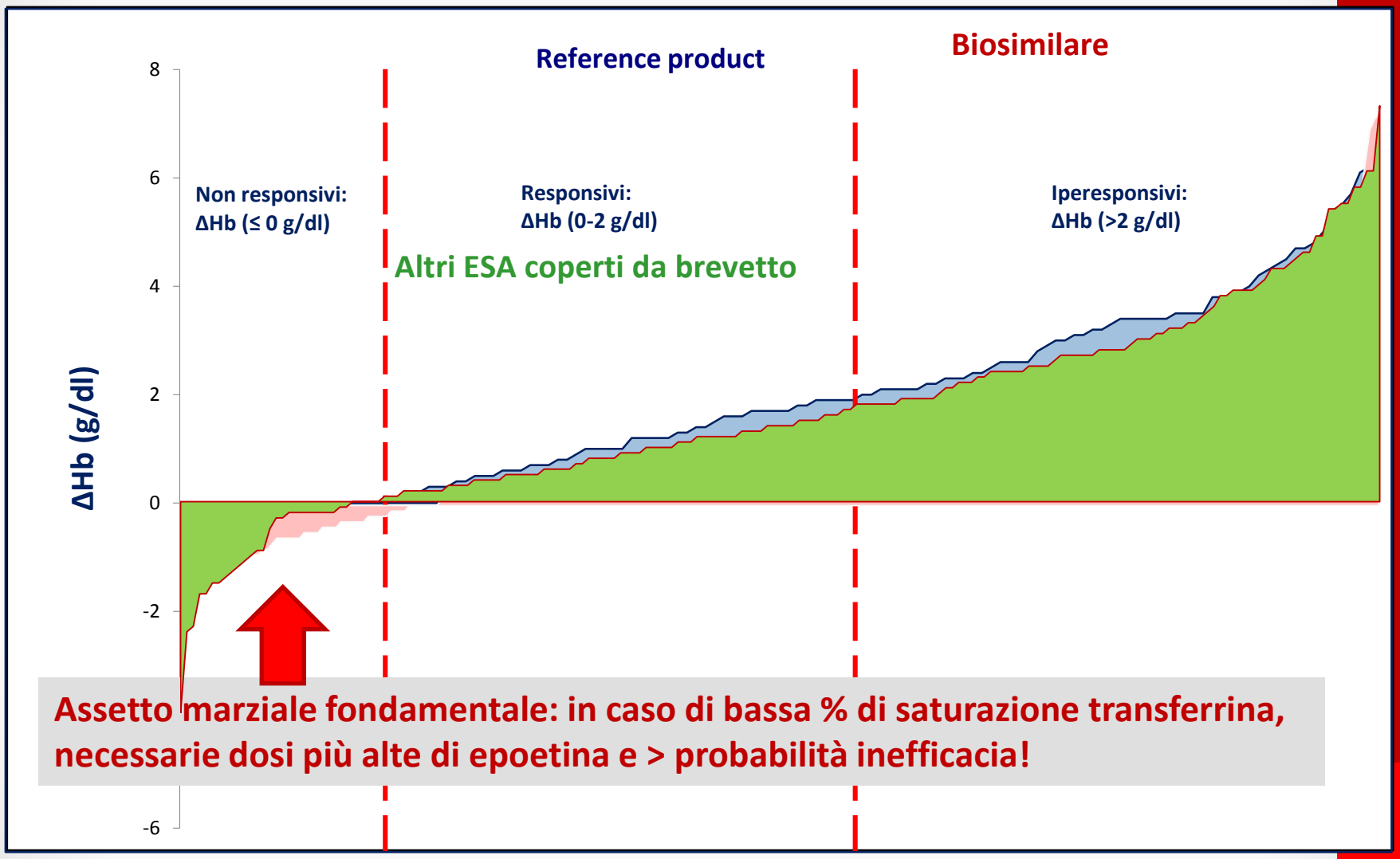
Uptake of biosimilar ESAs in different Italian Regions over time

% biosimilar on total epoetin users



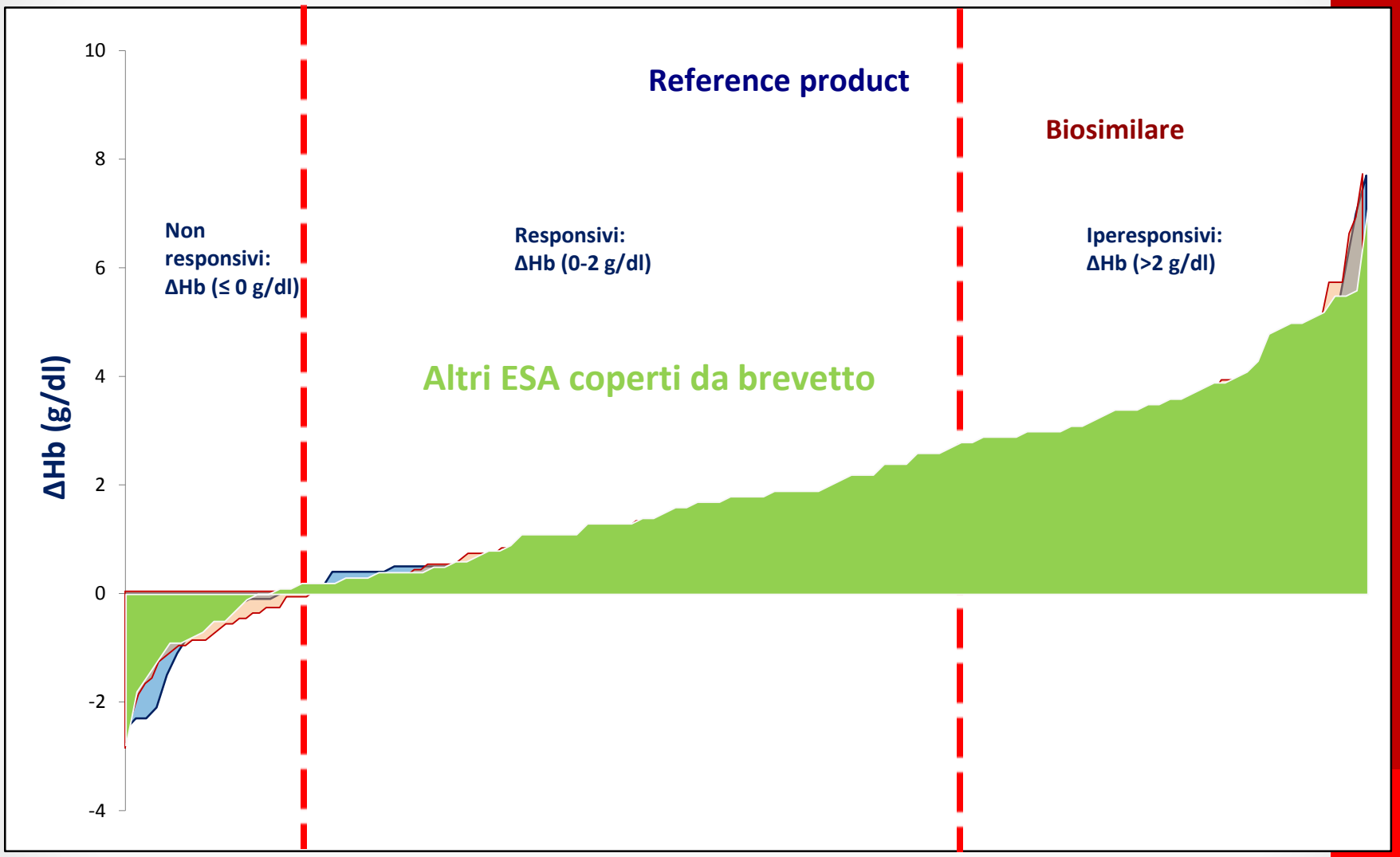
Ingrasciotta Y et al. How Much Are Biosimilars Used in Clinical Practice? A Retrospective Italian Population Study of Erythropoiesis-Stimulating Agents in the Years 2009-2013. BioDrugs. 2015 Aug;29(4):275-84

Responsività a terapia con biosimilari, reference product ed altri epoetine coperte da brevetto nei pazienti con IRC



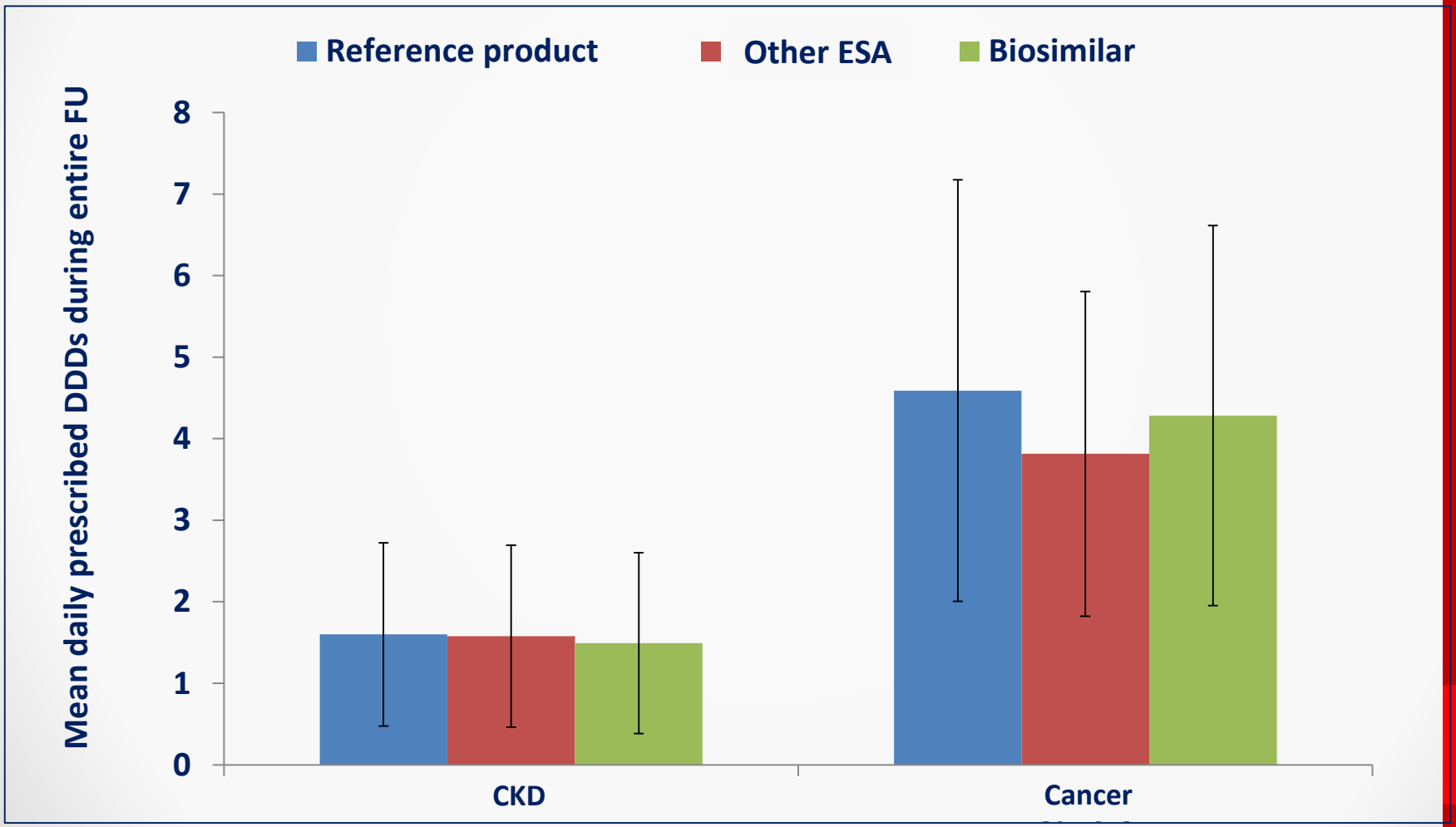
Risultati confermati nelle analisi aggiustate per potenziali fattori di confondimento

Responsività a terapia con biosimilari, reference product ed altri epoetine coperte da brevetto nei pazienti con cancro



Risultati confermati nelle analisi aggiustate per potenziali fattori di confondimento

Mean daily dose of different ESAs within 3 months after treatment start

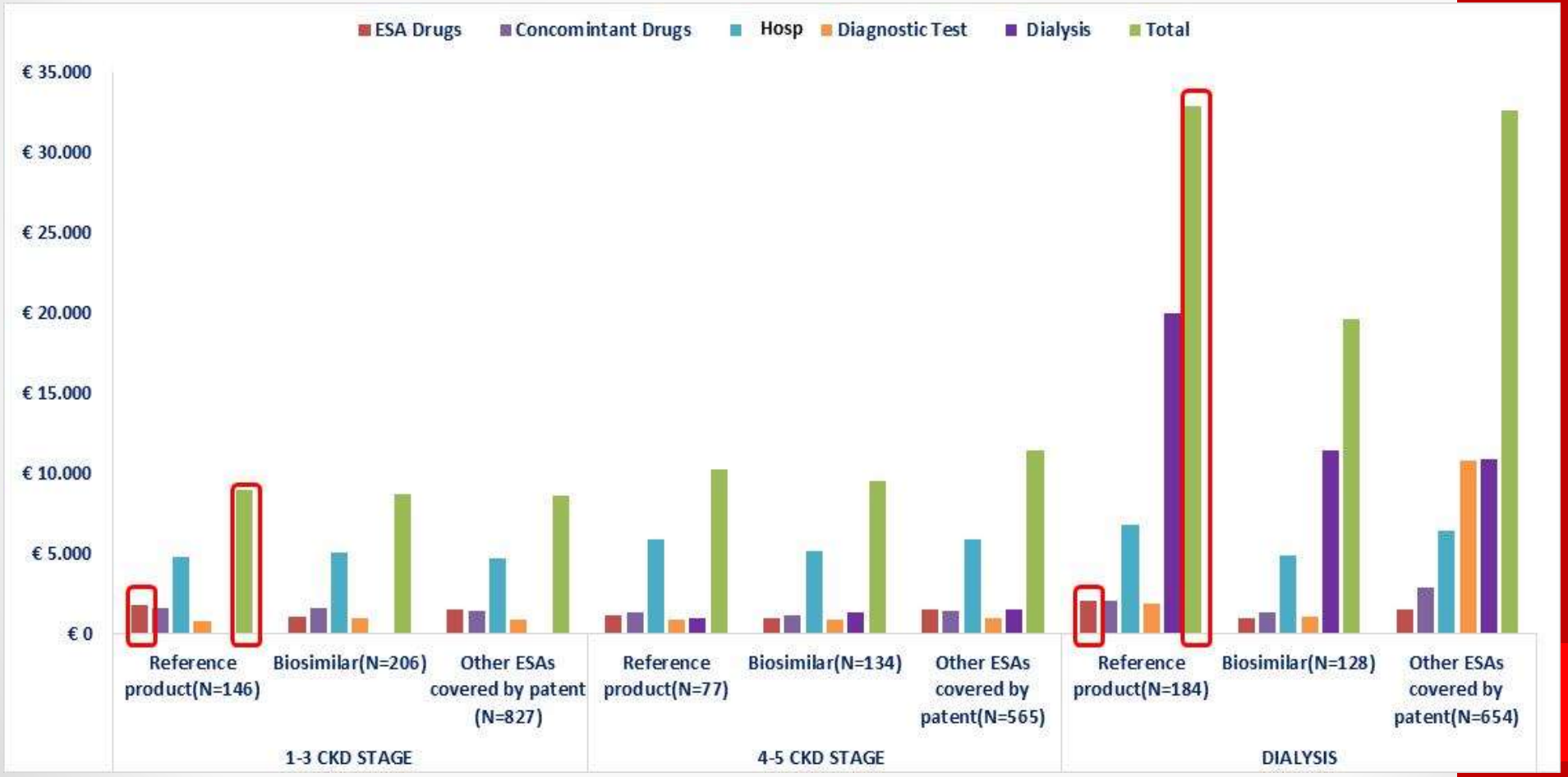


N. Epoetin users= 1,727 (Treviso LHU)

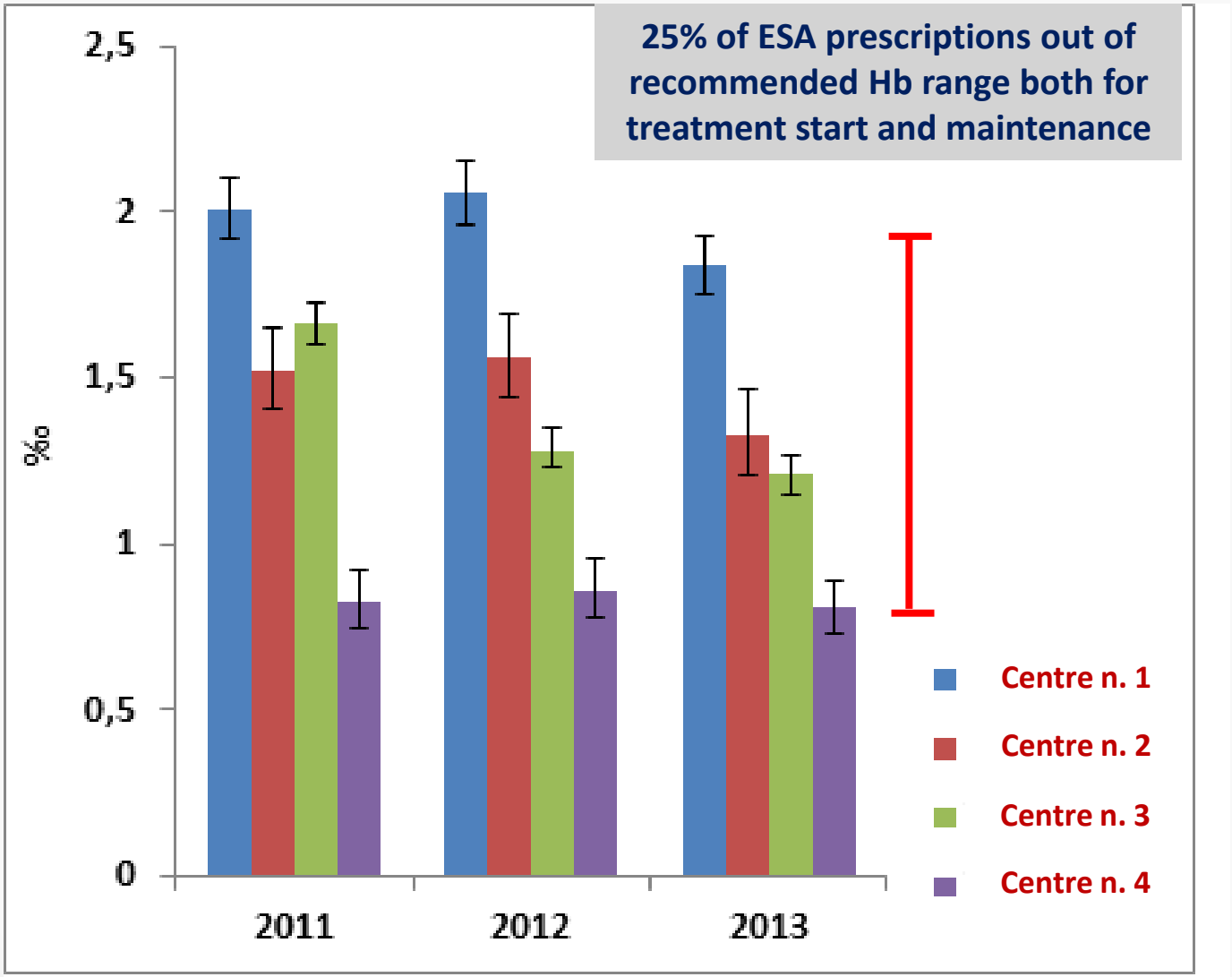
PLoS One. 2016 May 17;11(5):e0155805

Mean cost (€) per patient during the first year of ESA treatment, stratified by ESA type of and CKD severity

1-3 CKD stage:=1,179 (40.3%)
4-5 CKD stage: N=776 (26.6%)
Dialysis: N=966 (33.1%)

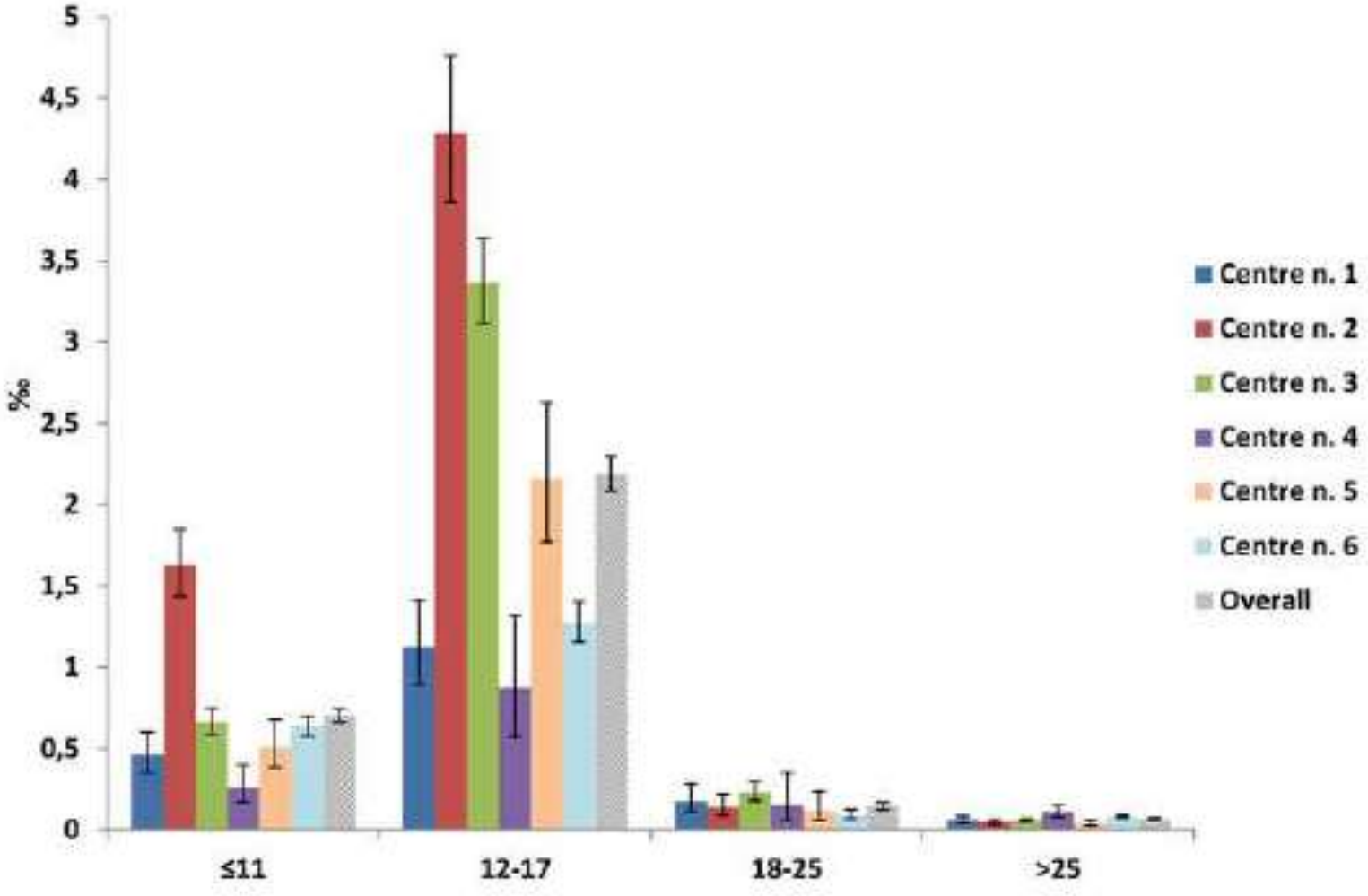


Age-adjusted prevalence of epoetin users per 1,000 inhabitants, stratified by calendar year and center



Ingrasciotta Y *et al. How Much Are Biosimilars Used in Clinical Practice? A Retrospective Italian Population-Based Study of Erythropoiesis-Stimulating Agents in the Years 2009-2013. BioDrugs. 2015;29(4):275-84.*

Age group specific prevalence of somatotropin use per 1,000 inhab. in the years 2009-2014, stratified by center



Siamo sicuri che i biosimilari sono sicuri?

- Gli **studi pubblicati** finora sulla maggior parte delle indicazioni non hanno mai suggerito una **non-sovrapponibilità tra biosimilare e originator**;
- Sono stati eseguiti e, talvolta pubblicati, i **Post Authorization Safety Study (PASS)** obbligatori ed altre valutazioni di FV obbligatorie senza che l'EMA ritenesse opportuno intervenire per modificare le condizioni di commercializzazione dei singoli biosimilari;
- Sono stati sottomessi ed esaminati da parte dell'EMA diversi **PSURs** e non sono emerse criticità tali da far ravvisare all'EMA motivi per ritornare sulla sua posizione di sovrapponibilità.

Società Italiana di Farmacologia. Revisione della posizione sui farmaci biosimilari da parte della Società Italiana di Farmacologia: Working Paper 2014. 2014. Disponibile online: http://www.sifweb.org/docs/sif_position_paper_revisione_biosimilari_lug14.pdf.

Comunicazione su andamento segnalazioni di sospette ADR da medicinali equivalenti e biosimilari (17/09/2014)

Agenzia Italiana del Farmaco

AIFA

Comunicazione su andamento delle segnalazioni di sospette reazioni avverse da medicinali equivalenti e biosimilari

Da un'analisi effettuata sui dati registrati, nel primo semestre del 2014, nella Rete Nazionale di Farmacovigilanza (RNF) , è emerso uno sproporzionato aumento del numero di segnalazioni di sospette reazioni avverse per alcuni principi attivi per i quali è scaduto il brevetto e quindi esistono i medicinali equivalenti e biosimilari.

Nella quasi totalità dei casi si tratta di segnalazioni che contengono reazioni avverse non gravi ed attese ad esempio disturbi gastrointestinali o reazioni allergiche lievi.

L'aumento di queste segnalazioni può essere ricollegato a vari fattori tra i quali una maggiore consapevolezza e sensibilità degli operatori sanitari verso l'importanza della segnalazione delle sospette reazioni avverse, come anche l'attivazione di progetti di farmacovigilanza e specifiche disposizioni regionali che possono influenzare il fenomeno.

La maggior parte di queste segnalazioni proviene da medici che non avevano mai segnalato una reazione avversa prima del 2014 e da Regioni in cui sono stati stipulati accordi attraverso i quali sostanzialmente il farmacista è autorizzato a non sostituire il prodotto originator con l'equivalente o biosimilare a patto che il paziente sia intollerante a quest'ultimo e che ciò sia dimostrato dall'inserimento nella RNF dell'apposita scheda di segnalazione di sospetta reazione avversa.

Si fa presente che qualsiasi dato contenuto nella Rete Nazionale di Farmacovigilanza dopo pochi giorni viene trasmesso alla banca dati europea Eudravigilance a cui accedono tutte le Agenzia regolatorie europee.

Si invitano, pertanto, tutti gli operatori sanitari ad una segnalazione responsabile focalizzata non soltanto su alcune specifiche tipologie di medicinali.

Farmaci biosimilari ed originator sono intercambiabili?

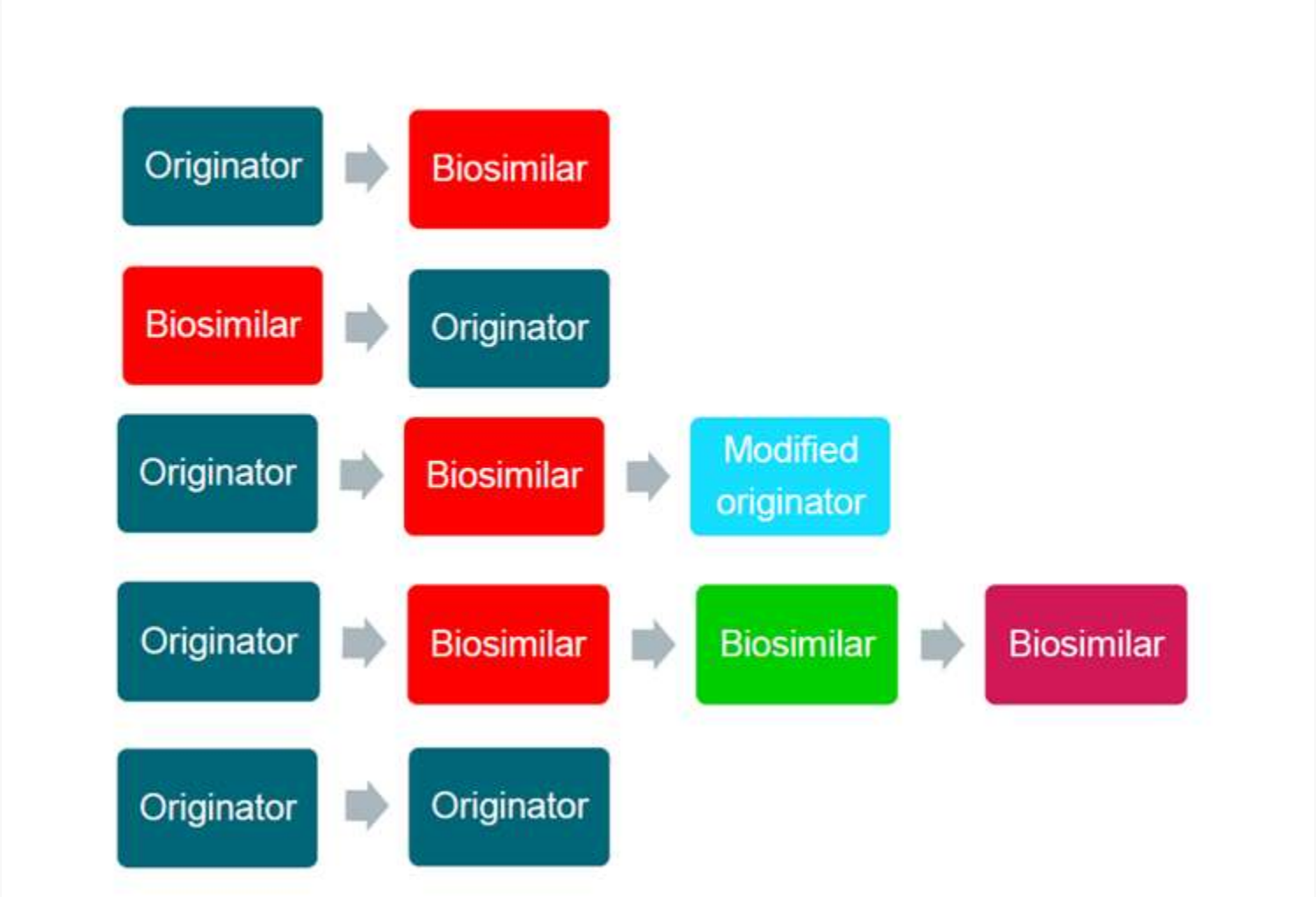
Definitions

- **Interchangeability:** possibility of exchanging one medicine for **another medicine** that is expected to have the **same clinical effect**. This could mean replacing a reference product with a biosimilar (or vice versa) or replacing one biosimilar with another;

- **Switching:** it is when the **prescriber** decides to exchange one medicine for another medicine with the **same therapeutic intent**;

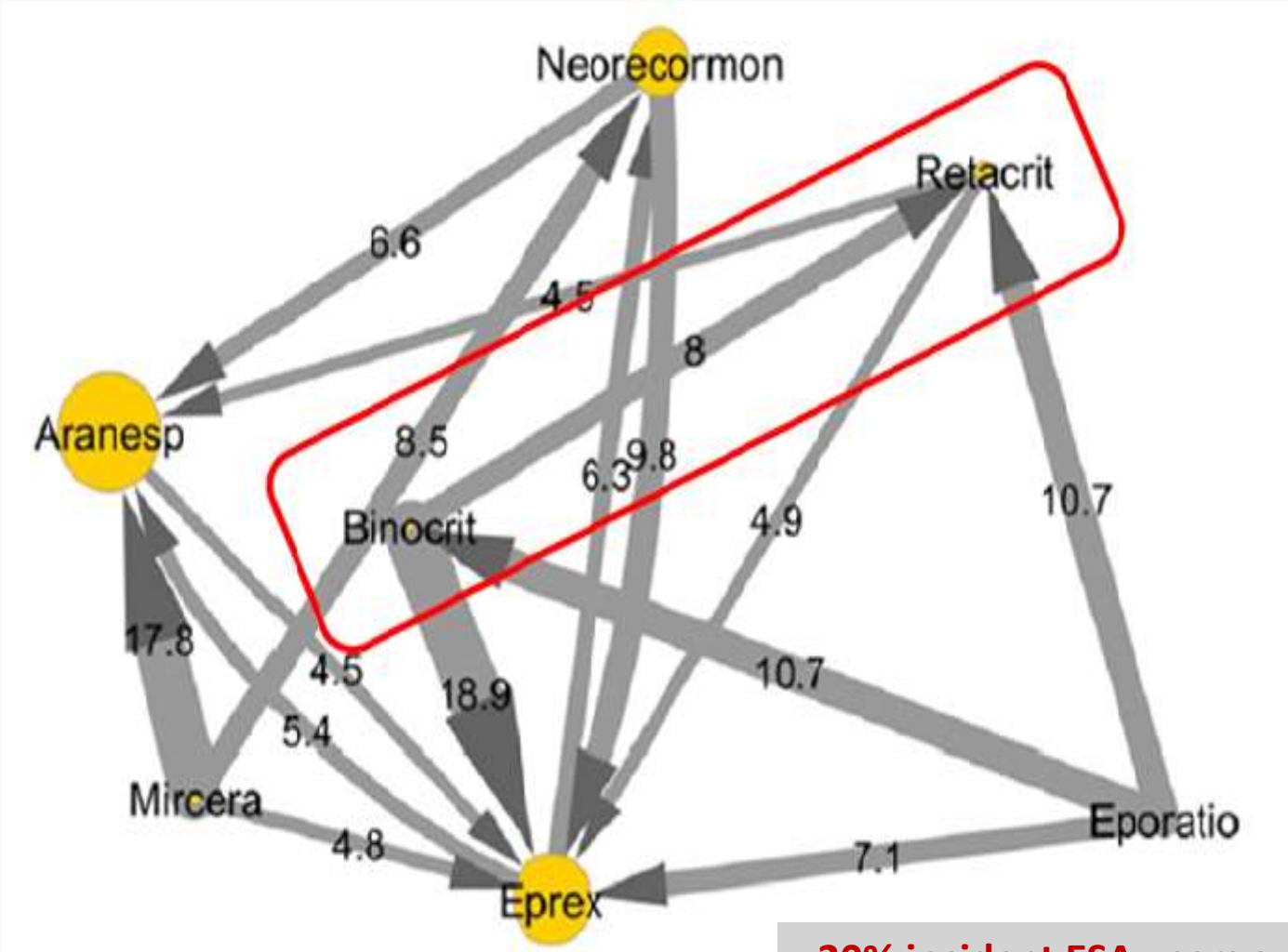
- **Substitution (automatic)**: the practice of **dispensing** one medicine instead of another equivalent and **interchangeable** medicine at pharmacy level **without consulting the prescriber.**

Switching will be an increasingly a complex issue



Adapted by presentation from S. Madsen (Norway Drug Agency) – 15th Medicines for Europe conference on Biosimilars - London 23-24/3/17

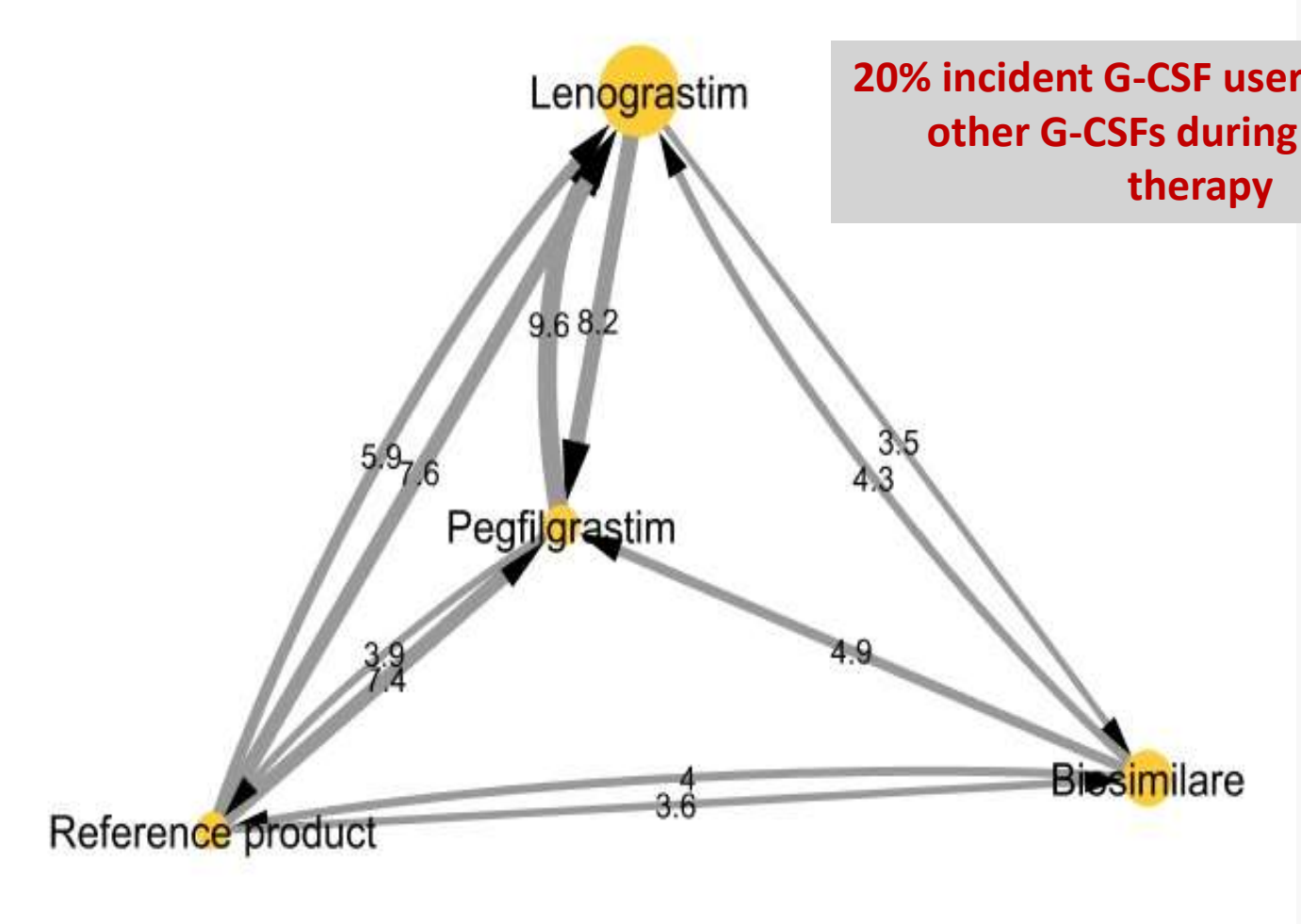
Switch between various ESAs during first year of therapy in 5 Italian Regions, years 2009-2014



Ingrasciotta Y *et al. How Much Are Biosimilars Used in Clinical Practice? A Retrospective Italian Population-Based Study of Erythropoiesis-Stimulating Agents in the Years 2009-2013. BioDrugs. 2015;29(4):275-84.*

20% incident ESA users switched to other ESAs during first year therapy

Switch between various G-CSFs during first year of therapy in 5 Italian Regions, years 2009-2014



20% incident G-CSF users switched to other G-CSFs during first year therapy

***Marcianò I** et al. How did the Introduction of Biosimilar Filgrastim Influence the Prescribing Pattern of Granulocyte Colony-Stimulating Factors? Results from a Multicentre, Population-Based Study, from Five Italian Centres in the Years 2009-2014. BioDrugs. 2016;30(4):295-306.*

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COMUNICATO STAMPA - Responsabilità editoriale di Business Wire

Celltrion Healthcare: NOR-SWITCH, lo studio indipendente del governo norvegese, sostiene il passaggio al biosimilare infliximab dal farmaco originale

I dati presentati all'edizione 2016 della UEG Week confermano che il passaggio al biosimilare infliximab non è inferiore al trattamento continuativo con il prodotto originale e che il risparmio sui costi può migliorare l'accesso da parte dei pazienti

Business Wire 19 ottobre 2016 09:22

https://www.ansa.it/sito/notizie/economia/business_wire/news/2016-10-19_119963409.htm

Review

EXPERT OPINION

1. Introduction
3. Safety databas
4. Current knowl switching
5. Discussion
6. Expert opinion

The safety of switching between therapeutic proteins

Hans C Ebbers, Michael Muenzberg & Huub Schellekens†
†*Utrecht University, Utrecht Institute for Pharmaceutical Sciences (UIPS), Department of Pharmaceutics, TB Utrecht, The Netherlands*

"We have found no evidence from clinical trial data or post marketing surveillance data that switching to and from different biopharmaceuticals leads to safety concerns."

t years has witching to may lead to f switching. related to thropoietins rom clinical trials, pharmacovigilance databases and an overview of the literature on the frequency of switching between these products. The review covers both switching between innovator products within the same product class and switching to and from biosimilars.

Expert opinion: Data on the frequency of switching in clinical practice is scarce, but it seems most frequent for erythropoietins. We have found no evidence from clinical trial data or post marketing surveillance data that switching to and from different biopharmaceuticals leads to safety concerns.

Ebbers et al. Expert Opin Biol Ther. 2012;12(11):1473-85

BioDrugs
DOI 10.1007/s40259-017-0210-0

CURRENT OPINION

Interchangeability of Biosimilars: A European Perspective

Pekka Kurki[1] · Leon van Aerts[2] · Elena Wolff-Holz[3] · Thijs Giezen[4] · Venke Skibeli[5] · Martina Weise[6]

"Our conclusion is that a state-of-the-art demonstration of biosimilarity, together with intensified post-marketing surveillance, is a sufficient and realistic way of ensuring interchangeability of EU-approved biosimilars under supervision of the prescriber."

Kurki et al. 2017 Gastroenterology. BioDrugs 2017 ePub

Indagine civica

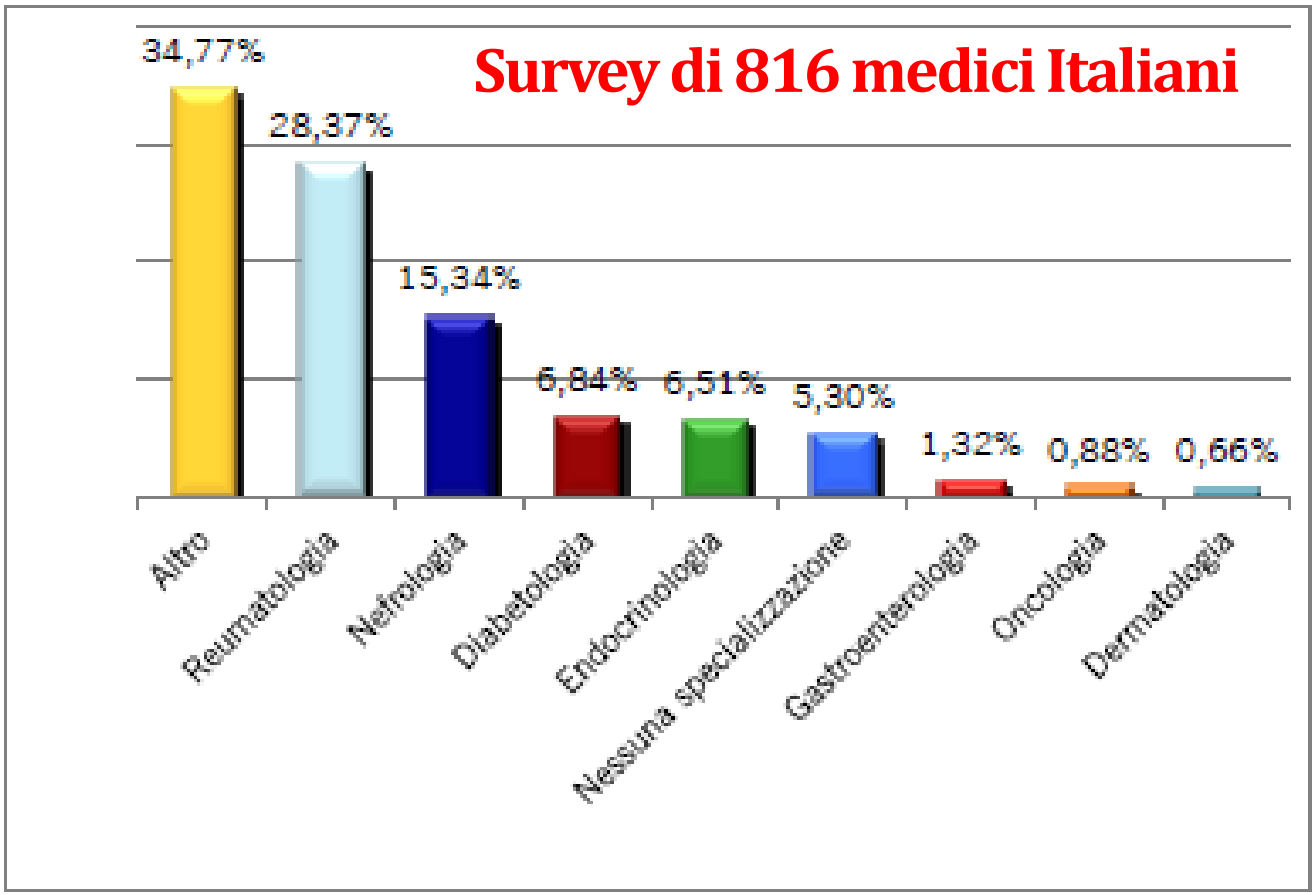
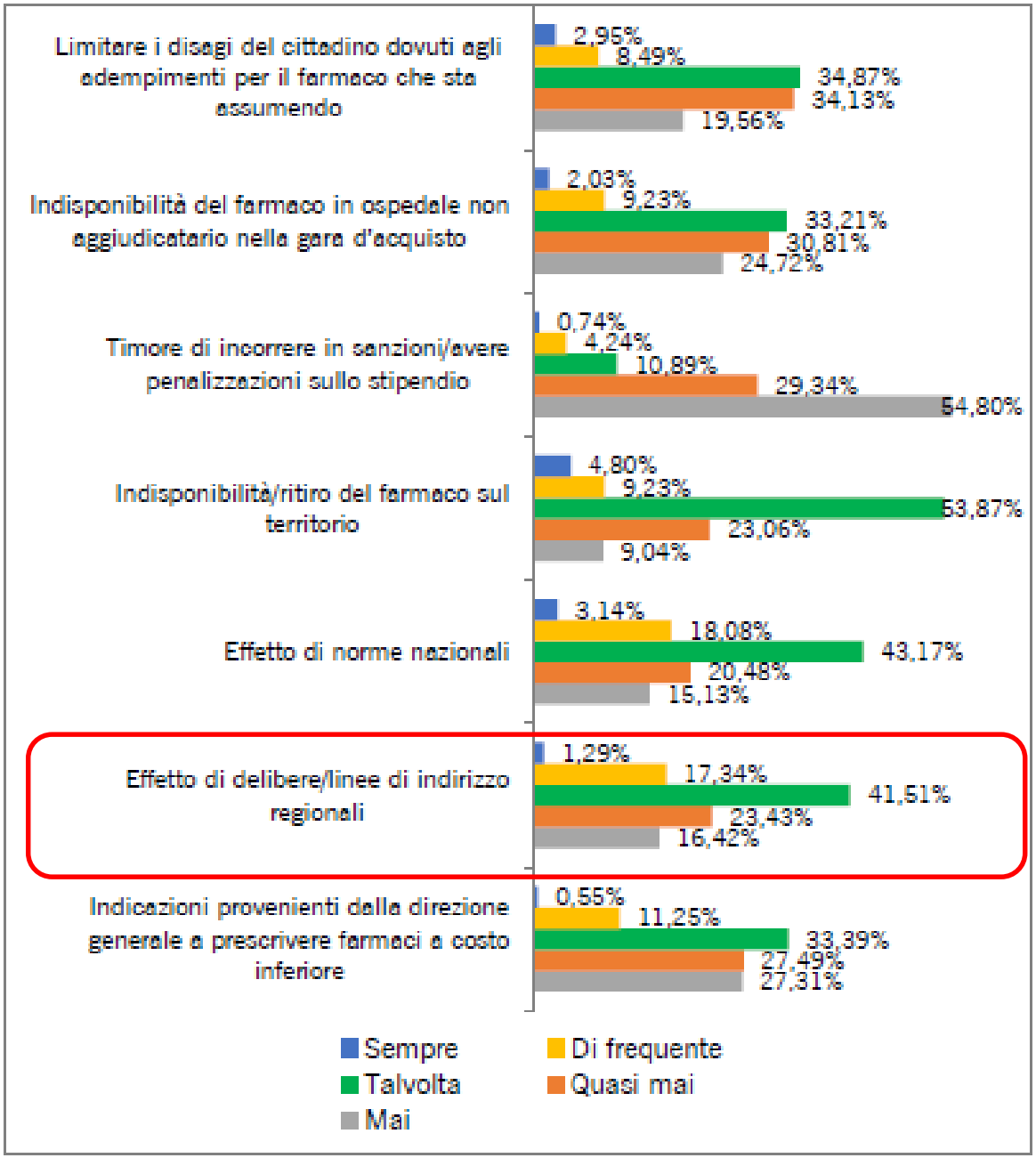


FIG.23 - NELLA SUA ESPERIENZA, LE POTREBBE ESSERE CAPITATO DI CAMBIARE/SOSTITUIRE LA TERAPIA A UN PAZIENTE. PER QUALI MOTIVI ORGANIZZATIVI/AMMINISTRATIVI?



Per un utilizzo consapevole e responsabile dei biosimilari informazione e formazione operatori sanitari è molto più importante di sanzioni, premialità e decreti!

Riflessioni conclusive

- Per rendere **sostenibile l'innovazione terapeutica** devono essere adottate molteplici strategie tra cui **utilizzo farmaci biologici a più basso costo**;

- Utile promuovere uso farmaci biosimilari....**solo se usati appropriatamente!**

- **Reti e banche dati sanitarie** sono strumento fondamentale per il **monitoraggio** profilo beneficio-rischio ed **appropriatezza uso** dei farmaci biologici/biosimilari tramite ***real world data***;

- **Operatori sanitari, decisori e pazienti** devono contribuire insieme alla generazione della **Real World Evidence sui biosimilari**.

#3F

& Real World Data

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Thanks for the attention

"The human mind is like a parachute. It works better when it is open". Paul Jansen

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Open Access Review

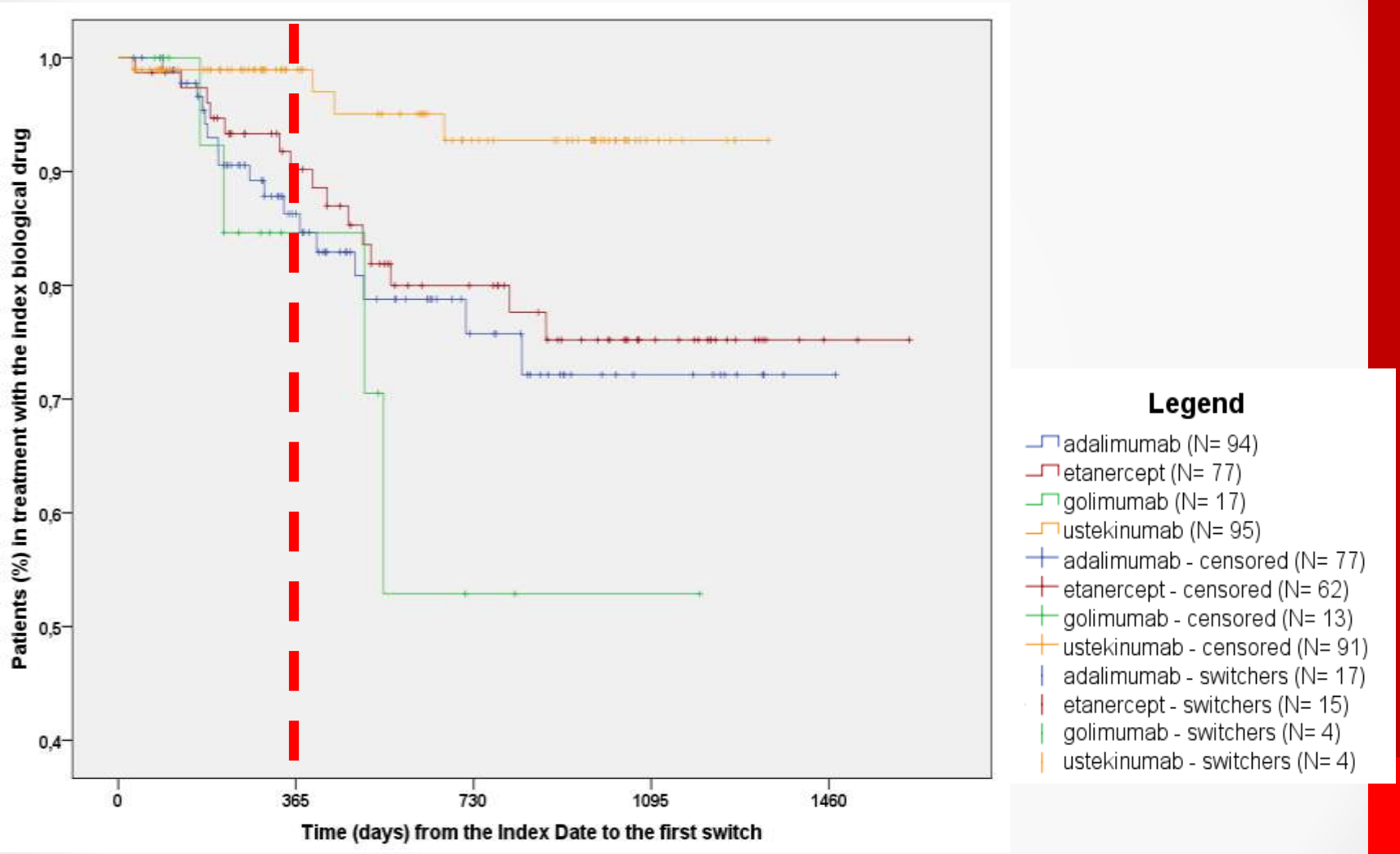
ESMO Open
Cancer Horizons

Biosimilars: a position paper of the European Society for Medical Oncology, with particular reference to oncology prescribers

Josep Tabernero,[1] Malvika Vyas,[2] Rosa Giuliani,[3] Dirk Arnold,[4] Fatima Cardoso,[5] Paolo G Casali,[6] Andres Cervantes,[7] Alexander MM Eggermont,[8] Alexandru Eniu,[9] Jacek Jassem,[10] George Pentheroudakis,[11] Solange Peters,[12] Stefan Rauh,[13] Christoph C Zielinski,[14] Rolf A Stahel,[15] Emile Voest,[16] Jean-Yves Douillard,[2] Keith McGregor,[2] Fortunato Ciardiello[17]

- With potential savings, a rapidly increasing range of biologic products and well-informed healthcare professionals and patients, **biosimilars do represent one of the ways forward to obtain sustainability**;
- Physicians will make decisions based on what is best for their patients. To ensure that the decision is accurate, **information is crucial for the prescriber, pharmacist, nurse and patient;**
- Collecting enough **data**, including findings from **clinical studies**, to instill **confidence** in prescribers, pharmacists and patients concerning the medicinal product and patient **monitoring** via expert teams will be crucial in the field of biosimilar medicinal products.

Time-to-switch of biological drugs in PsO/PsA patients



Legend: PsO= psoriasis; PsA= psoriatic arthritis; q1-q3= Interquartile range.
Only non sporadic users (at least one dispensing of one of the study drugs within 1 year after the index date) were included (N= 285).
Due to low number, infliximab users (N= 2) are not included in the Kaplan Meier curve.

Future challenges

- To explore comparative **long-term safety and effectiveness** of first generation biosimilars thanks to data that have been cumulated over time;
- To evaluate **clinical effects of switch** between originator and biosimilars and **viceversa** and between different originators;
- To consider secondary use of **healthcare databases** for post-marketing surveillance also of **second generation biosimilars** in **cancer patients;**
- While promoting use of **low cost biologicals**, do no forget that **prescribing wisely** biologicals is the highest priority as cost containing strategy;
- **Payers, healthcare professionals and patients** have to be all involved in the **RWE generation** about biosimilars to be **integrated with premarketing RCT** evidence;
- In light of growing number of biosimilars to be marketed in near future in several therapeutic areas, to establish an **international post-marketing surveillance system for biosimilars** specifically.

ECCO Position Statement on the Use of Biosimilars for IBD

1. A biosimilar product registered in the EU is as efficacious as the reference product when used in accordance with the Summary of Product Characteristics.

2. Demonstration of safety of biosimilars requires large observational studies with long-term follow-up in IBD patients, supplemented by registries.

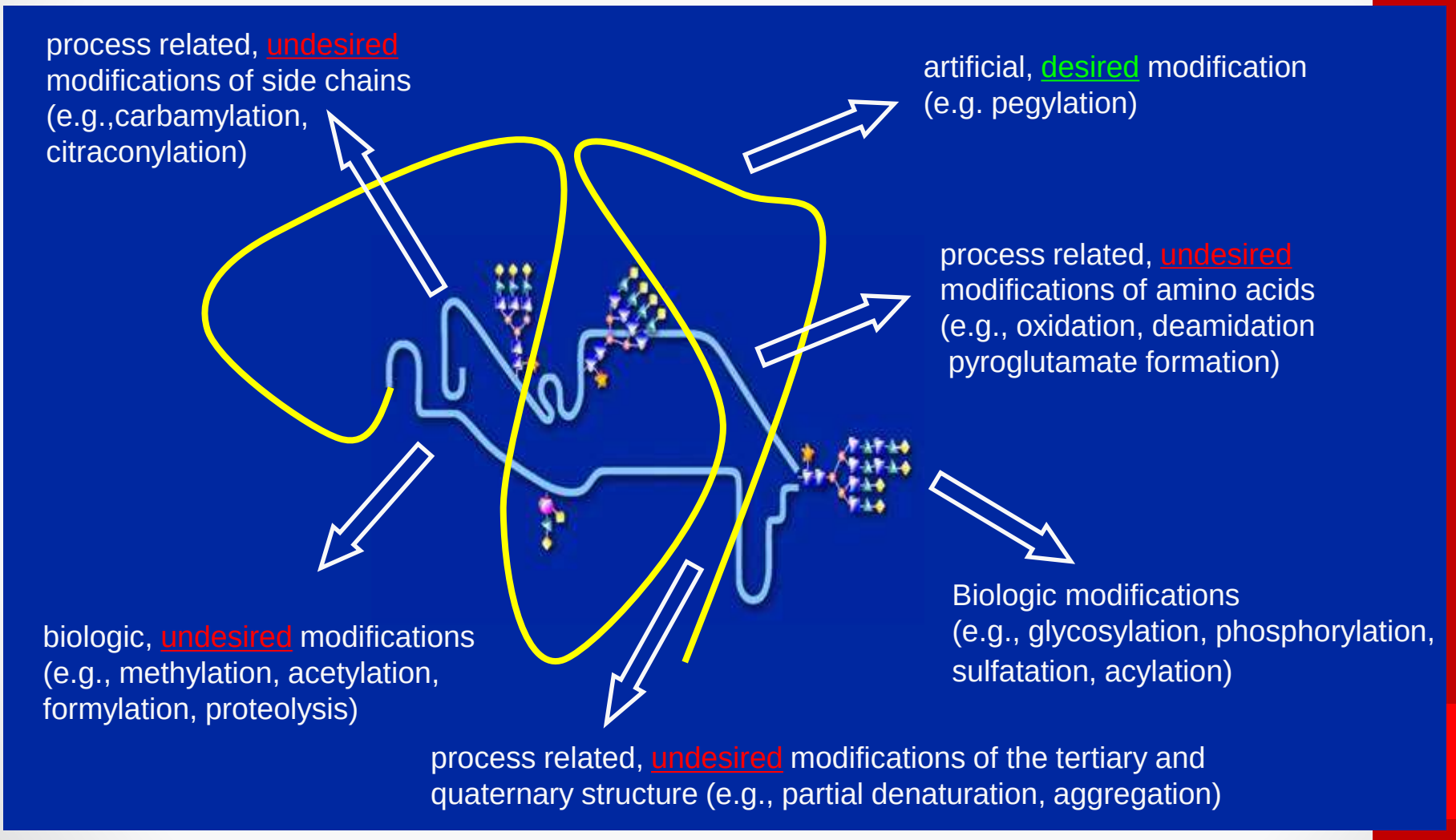
3. As for all biologics, traceability should be based on a robust pharmacovigilance system and the risk management plan.

4. Switching from the originator to a biosimilar in patients with IBD is acceptable. Studies of switching can provide valuable evidence for safety and efficacy. Scientific and clinical evidence is lacking regarding reverse switching, multiple switching, and cross-switching among biosimilars in IBD patients.

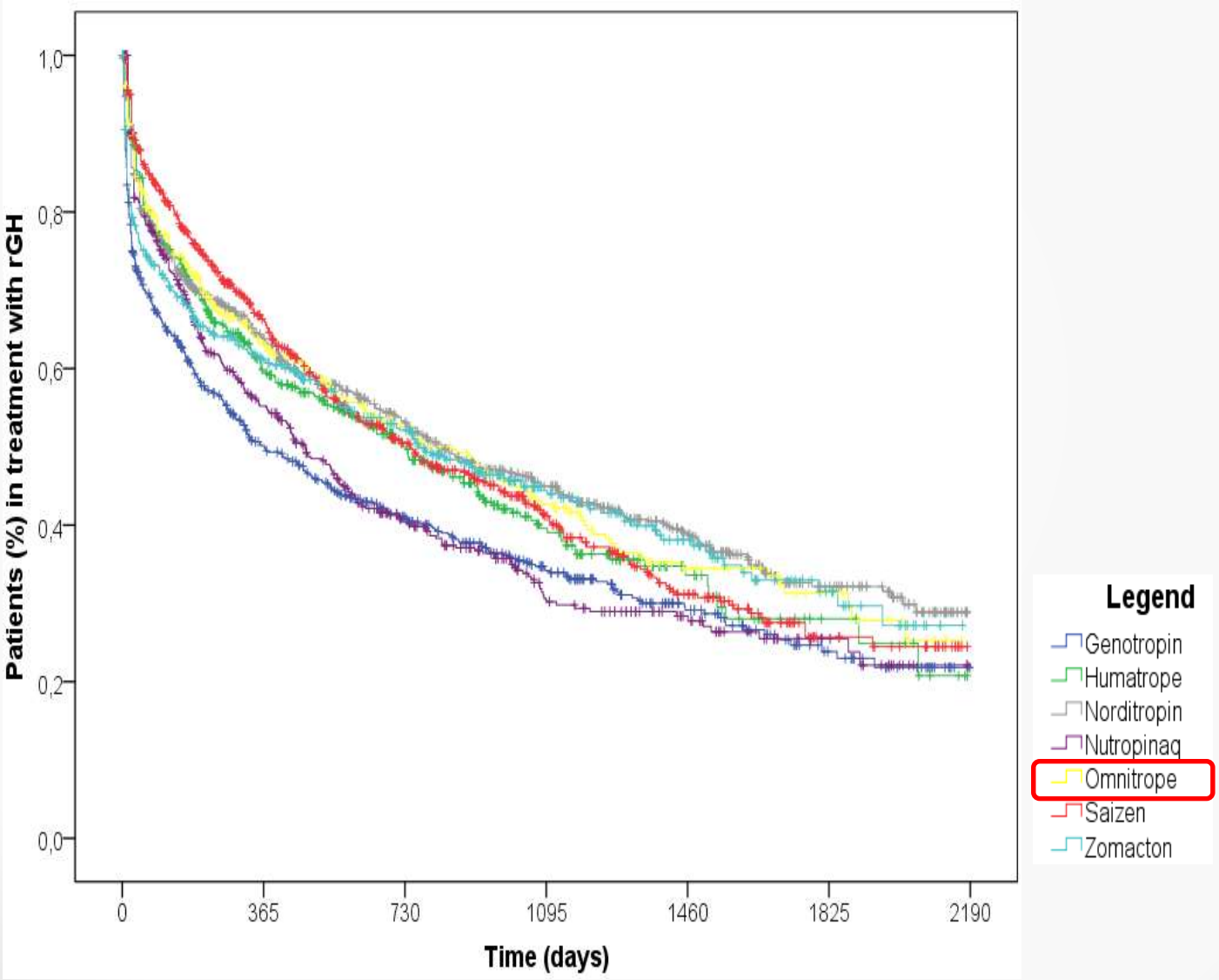
5. Switching from originator to a biosimilar should follow appropriate discussion between physicians, nurses, pharmacists, and patients.

Danese S *et al. ECCO Position Statement on the Use of Biosimilars for Inflammatory Bowel Disease-An Update. J Crohns Colitis. 2017 Jan;11(1):26-34.*

Microeterogeneità di proteine terapeutiche collegate alla biologia del prodotto ed al processo produttivo



Time to discontinuation of rGH therapy among naïve users, stratified by medicinal product



Interchangeability

Europe

Interchangeability[1]

- A scientific and medical term
- The medical practice of changing one medicine for another that is expected to achieve the same clinical effect in a given clinical setting and in any patient on the initiative, or with the agreement of the prescriber

Substitution

- An administrative measure
- Practice of dispensing one medicine instead of another equivalent and interchangeable medicine at the pharmacy level without consulting the prescriber

[1] European Commission 2013: What you need to know about biosimilar medicinal products. http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_report_en.pdf

United States

Interchangeable or **Interchangeability:**

- the biological product is **biosimilar** to the reference product;
- it can be expected to produce the **same clinical result** as the reference product **in any given patient**; and
- for a product that is administered more than once to an individual, the risk in terms of **safety or diminished efficacy of alternating or switching** between use of the product and its reference product is not greater than the risk of using the reference product without such alternation or switch.

An interchangeable product **may be substituted** for the reference product without the intervention of the health care provider who prescribed the reference product.