MINISTERIO
DE SANIDAD, SERVICIOS SOCIALES
E IGUALDAD

agencia española de
medicamentos y
productos sanitarios

Biosimilares

Sol Ruiz

AEMPS - 3 mayo 2017


QSE
reference
biosimilar
comp
studies

How to establish biosimilarity?

1. extensive characterization
(physico-chemical-biological)

***2. in vitro* functional activity**
(MoA of the molecule)

***3.* efficacy and safety studies**
('best' population)

1	Medicine Name	Active Substance	Status	Authorisation date
2	Alpheon	rHu IFN alfa-2a	Refused	-
3	Filgrastim ratiopharm	filgrastim	Withdrawn	15/09/2008
4	Amgevita	adalimumab		22/03/2017
5	Valtropin	somatropin	Withdrawn	24/04/2006
6	Ovaleap	follitropin alfa		27/09/2013
7	Ratiograstim	filgrastim		15/09/2008
8	Tevagrastim	filgrastim		15/09/2008
9	Biograstim	filgrastim	Withdrawn	15/09/2008
10	Thorinane	enoxaparin sodium		15/09/2016
11	Omnitrope	somatropin		12/04/2006
12	Grastofil	filgrastim		18/10/2013
13	Accofil	filgrastim		18/09/2014
14	Silapo	epoetin zeta		18/12/2007
15	Solumarv	insulin human	Refused	-
16	Lusduna	insulin glargine		04/01/2017
17	Solymbic	adalimumab		22/03/2017
18	Epoetin Alfa Hexal	epoetin alfa		28/08/2007
19	Flixabi	infliximab		26/05/2016
20	Binocrit	epoetin alfa		28/08/2007
21	Abseamed	epoetin alfa		28/08/2007
22	Bemfola	follitropin alfa		27/03/2014
23	Terrosa	teriparatide		04/01/2017
24	Truxima	rituximab		17/02/2017
25	Zarzio	filgrastim		06/02/2009
26	Inflectra	infliximab		10/09/2013
27	Abasaglar (prev Abasria)	insulin glargine		09/09/2014
28	Retacrit	epoetin zeta		18/12/2007
29	Benepali	etanercept		14/01/2016
30	Remsima	infliximab		10/09/2013
31	Filgrastim Hexal	filgrastim		06/02/2009
32	Movymia	teriparatide		11/01/2017
33	Nivestim	filgrastim		08/06/2010
34	Inhixa	enoxaparin sodium		15/09/2016

News

21/04/2017

Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 18-21 April 2017

Eleven medicines recommended for approval, including four orphans

Three biosimilar medicines were recommended for approval by the Committee: **Erelzi** (etanercept) for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis, plaque psoriasis and paediatric plaque psoriasis; and **Rixathon** and **Riximyo**, both containing rituximab, for the treatment of non-Hodgkin's lymphoma, rheumatoid arthritis, granulomatosis with polyangiitis and microscopic polyangiitis. Rixathon is also intended for the treatment of chronic lymphocytic leukaemia. A biosimilar medicine is a biological medicine that is highly similar to another biological medicine that is already authorised for use.

for the treatment of Wilson's disease, a rare autosomal recessive inherited disorder.
Hybrid applications rely in part on the results of pre-clinical tests and clinical trials for a reference product and in part on new data. Cuprior has an orphan designation.

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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

2015

Quality 101

- Same aa sequence, posology and RoA
- Strength, pharmaceutical form, and formulation may differ
- Molecular differences to enhance E not allowed

LA EXTRAPOLACION DE INDICACIONES NO ES UN CONCEPTO NUEVO

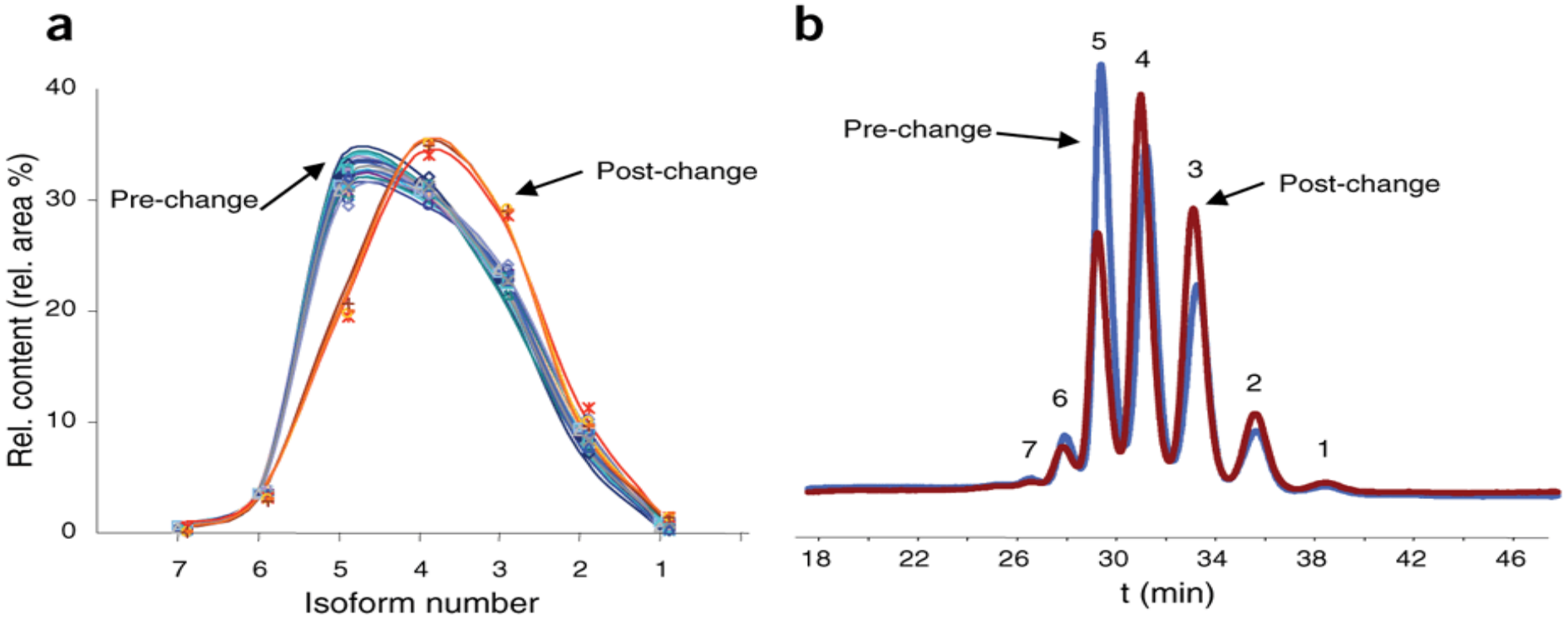

Figure 1 Comparison of the pre- and post-change Aranesp batches measured by capillary zone electrophoresis. (**a**) Relative content of the individual isoforms of the pre-change ($n = 18$) and the post-change ($n = 4$) batches. (**b**) Representative electropherograms; peaks are labeled with the isoform number.

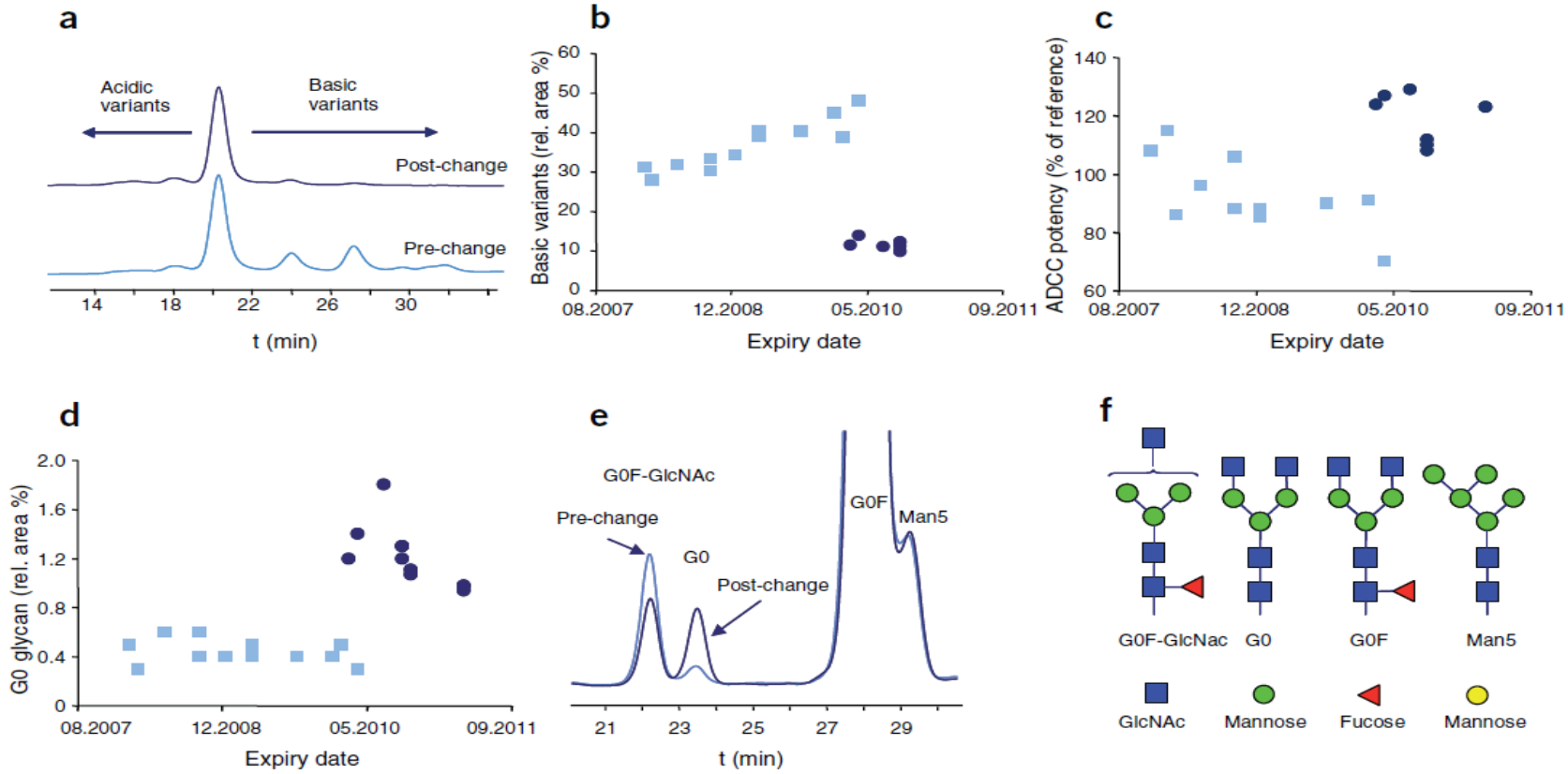

Figure 2 Comparison of the different pre- and post-change batches of Rituxan/Mabthera. (**a**) Exemplary CEX chromatograms. (**b**) Amount of basic variants of the pre-change ($n = 12$) and post-change ($n = 6$) batches as measured by CEX. (**c**) ADCC potency of the pre-change ($n = 11$) and post-change ($n = 8$) batches. (**d**) Relative amount of the G0 glycan of the pre-change ($n = 13$) and post-change ($n = 11$) batches. (**e**) Exemplary glycan mapping chromatogram (**f**) Glycan legend.

Another example where extrapolation has already been accepted is the introduction of a new subcutaneous (SC) formulation of a hitherto intravenously (IV) applied product. Although the formulation and bioavailability of the SC product will be different, one clinical study is usually sufficient to grant several, if not all, clinical indications approved for the IV product. This is illustrated by the recent approval of an SC formulation of an anti-Her2 monoclonal antibody (mAb) based on clinical data in the neoadjuvant setting, which were extrapolated to the metastatic setting based on the totality of the evidence from all data provided.[27] It is notable that the SC formulation of that antibody contains recombinant human hyaluronidase (rHuPH20) as a permeation enhancer and is thus considerably different from the IV formulation. A formulation difference of this magnitude would not be acceptable for a biosimilar compared with the reference product.

Extrapolación de indicaciones; considerar:

- Evidencia global del ejercicio de comparabilidad
- Posibles incertidumbres derivadas de los datos
- Perfil de seguridad aceptable (incluyendo inmunogenicidad)

CHALLENGES

- Very different expression system
- Variability of RMP vs Biosimilar; number of batches, EU vs US
- Use of statistical tools
- Concept applied to less characterized biologicals?

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gracias!

sruiz@aemps.es