



A Physician's consideration towards Biosimilars

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1ST NATIONAL BIO-THERAPEUTICS

Disclosure

I received unrestricted research grants or acted as a speaker for
Abbvie, Amgen, BMS, Celtrion, Celgene, Janssen, MSD, Novartis, Novo Nordisk,
Pfizer, Roche, Servier, UCB

Outline

- Clinical Discussion
- Overview of your opinions on biosimilar concepts
- The Portuguese Experience

Clinical Discussion

Clinical Vignette

- Male, 38 years old
- Plaque psoriasis and axial and peripheral arthritis
- Skin and joint refractory to methotrexate, cyclosporine, joint injections and NSAIDS
- Indication for anti-TNF treatment

Biologics Approved in Europe for Psoriasis

- TNF inhibitors
 - Infliximab
 - Adalimumab
 - Etanercept
- Ustekinumab
- Alefacept (not available in Europe)

Infliximab Biosimilar Approved in Europe

Studied in Rheumatoid Arthritis and Ankylosing Spondylitis

Not studied: *Psoriasis, Crohn's disease, UC, psoriatic arthritis*

Has approval for all these indications

Questions



1 The hospital has infliximab biosimilar available as a first-line anti-TNF due to economic reasons. What should be done?

1. Use infliximab biosimilar
2. Argue that infliximab biosimilar has almost no experience on this disease and ask for infliximab originator
3. Argue that the patient needs more independence and mobility and ask for adalimumab
4. Argue that the patient has a high risk of tuberculosis contact and ask for etanercept as it is apparently associated with a lower tuberculosis risk
5. Start ustekinumab as it is not an anti TNF and can be used as first line therapy in psoriasis and psoriatic arthritis

2

3 months later, the patient is responding well to this infliximab biosimilar, but now the hospital has a different infliximab biosimilar to offer. What should be done?

1. Switch to this infliximab biosimilar immediately
2. Argue that this is a very short period of time for switching because it doesn't allow to adequately track the use of this biosimilar in this patient and ask to keep the same for more 3 months
3. Argue that the patient is well on this infliximab biosimilar and that he should always keep the same one
4. Argue that the patient needs more independence and mobility and ask for adalimumab
5. Start ustekinumab as it is not an anti TNF and can be also used as first line in Psoriatic Arthritis

3 The patient switched to the other infliximab biosimilar, but 6 months later is losing the response. What should be done?

1. Switch to the previous infliximab biosimilar
2. Switch to infliximab originator
3. Increase dose and frequency
4. Switch to adalimumab
5. Dose drug and antibodies to infliximab and decide based on this

4 High titer of anti infliximab antibodies were detected and drug levels are very low. What should be done?

1. Switch to the previous infliximab biosimilar
2. Switch to infliximab originator
3. Increase dose and frequency
4. Switch to adalimumab
5. Switch to ustekinumab

5 Dose was increased as well as frequency but no response occurred. What should be done?

1. Switch to the previous infliximab biosimilar
2. Switch to infliximab originator
3. Introduce MTX
4. Switch to adalimumab
5. Switch to ustekinumab

Overview of Biosimilars

1 Before attending this scientific meeting, what was your knowledge level on biosimilars?

1. Never heard the term biosimilar
2. Heard the term and understand biosimilars to be the “generics” for biologics
3. Specific and in-depth knowledge about biosimilars

Manufacturing

What manufacturing information is most important to clinicians making treatment decisions?

Manufacturing

2 Do you believe that the manufacturing process is the key to the final product of a biotherapeutic molecule?

1. Yes
2. No
3. Partially agree

Indication Extrapolation

- How will indication extrapolation impact your practice when biosimilars become available, and when multiple biosimilars are available?
- What factors should be considered (beyond mechanism of action) when evaluating a product when only extrapolated data is available?
- Might you consider differences between treatment-naïve patients and treatment-experienced patients?
- Which diseases or conditions might you accept indication extrapolation?
- Which diseases or conditions might you reject indication extrapolation?
- What information do the Health Authorities and Regulatory Agencies need regarding indication extrapolation?

Indication Extrapolation

3 Do you feel that the mechanism of action of complex molecules such as monoclonal antibodies are not fully understood and it is difficult to define the most sensitive patient population in different therapy areas?

1. Yes
2. No
3. Unsure

Indication Extrapolation

4 Do you believe that the indication approval for a biosimilar compound should be granted and restricted only for the ones, which has sufficient comparability data against the innovator product?

1. Strongly agree
2. Agree
3. Disagree

Interchangeability

- What future research or clinical data do you need before deciding if a biosimilar product is appropriate to substitute?
- How will interchangeability impact your practice when biosimilars become available, and when multiple biosimilars are available?
- Is a single dose study adequate to determine interchangeability?
- Might you consider differences between treatment-naïve patients and treatment-experienced patients when considering substitution?

Interchangeability

5 Should a biosimilar manufacturer demonstrate therapeutic equivalence with a innovator product in switching or alternate studies, can it be interchanged with the innovator product in clinical practice, assuming to achieve the same effect in a given clinical setting and in any patient?

1. Agree
2. Disagree
3. Unsure

Pharmacovigilance

- What approaches should interdisciplinary teams take, such as hospital department leadership and purchasing pharmacists, regarding traceability?
- Once multiple biosimilars are available, how should pharmacies and physicians track or monitor which product is dispensed from the pharmacy?
- Do you believe there is a need to change how you report adverse events in the patient record?

Pharmacovigilance

6 How should biosimilars with the same INN be prescribed?

1. Brand name only
2. Brand and generic name
3. Generic name only

Pharmacovigilance

7

Do you agree that a distinguishable non-proprietary names for biosimilars enhance effective adverse events reporting and increase accurate prescribing?

1. Agree
2. Disagree
3. Partially agree

Drug Selection

8

When considering between a biosimilar and an innovator drug for an eligible patient, what is your primary selection criteria based on?

1. Patient safety
2. Cost and economic constraints
3. Robust evidence, including clinical trials, to be highly similar in term of efficacy and safety to the innovator medicines

The Portuguese Experience



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Methods for a Position Paper



- A systematic literature review of the clinical trials of the biosimilars that are positioned to be used in rheumatic diseases was performed.
- A systematic literature review of the International Position Papers on the use of biosimilar drugs was also carried out. We included the position of other medical, pharmaceutical and scientific organizations concerning the use of biosimilar drugs. The search was supplemented with a hand search through the websites of several international societies.
- The results of this evidence-based approach were presented and discussed during a national meeting of the Portuguese Society of Rheumatology (SPR). During the meeting, a first plenary session was dedicated to an open discussion and to the elaboration of a first draft of a bullet like SPR position on the use of biosimilars in the field of rheumatology. A steering committee made a final proposal of this position, which was adapted and approved in a second plenary meeting that took place in the following day.

Strategy for a Position Paper

- Publication together with a systematic review of the clinical trials
- Publication together with an editorial from an opinion leader
- Text send to all national and international stakeholders
- Presentation in heterogeneous forums, ranging from patients to politicians, national and international



P P P

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- This position statement is contrary to automatic substitution
- Defends either a different INN or the prescription by brand name
- Switching only based on physician decision and after patient information
- Recommends the registration of all biosimilar treated patients in Reuma.pt for efficacy, safety and immunogenicity surveillance, following the strategy already ongoing for originators
- Opposes to extrapolation of indications approved to the originator to completely different diseases and/or age groups without adequate preclinical, safety or efficacy data

INFORMAÇÃO: No formulário das terapêuticas, já podem ser registados os biossimilares do Infiximab.

Registo Nacional de Doentes Reumáticos Rheumatic Diseases Portuguese Register



Reuma.pt

Centro

Código de utilizador

Senha de acesso

[Recuperar dados](#)

Totais de doentes e consultas registados no



- Cirurgias e Procedimentos
- Patologias Associadas
- Avaliação da doença
- Articulações
- EVA / Índices Actividade
- HAQ
- EQ5D
- HADS
- SF36
- FACT
- Respostas ACR e EULAR
- Laboratório

Terapêuticas

Consulta 14 de 39, registada em 2009-10-12

Consultas: 2009-10-12_10:16

Pesquisa de Fármacos

Lista de Fármacos

Nome Comercial	DCI
Remicade	Infliximab
Remsima	Infliximab
Inflectra	Infliximab

ta Fim Terap.	Dose	Fr
10	15 miligramas	se
10	7,5 miligramas	d

List Details

Active ingredient **Infliximab**

Brand name **Inflectra**

Drug forms

Dosage	Route	Pharmaceutical forms
100 mg	Intravenous route	Powder for concentrate for sol

Start date (Today)

Regimen

Dosing frequency:

Dosage:

Dosage unit:

A cartoon character shaped like a bone, with a friendly face, large eyes, and a wide smile. It has yellow hands and feet. The character is holding a white rectangular sign on a wooden stick with its right hand. The sign has the word "Obrigado!" written in blue. Its left hand is raised with the index finger pointing upwards. The background is dark with some blue light effects.

Obrigado!

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