Review Article

Advances in Bioengineering & Biomedical Science Research

Biologics in Autoimmune Disease

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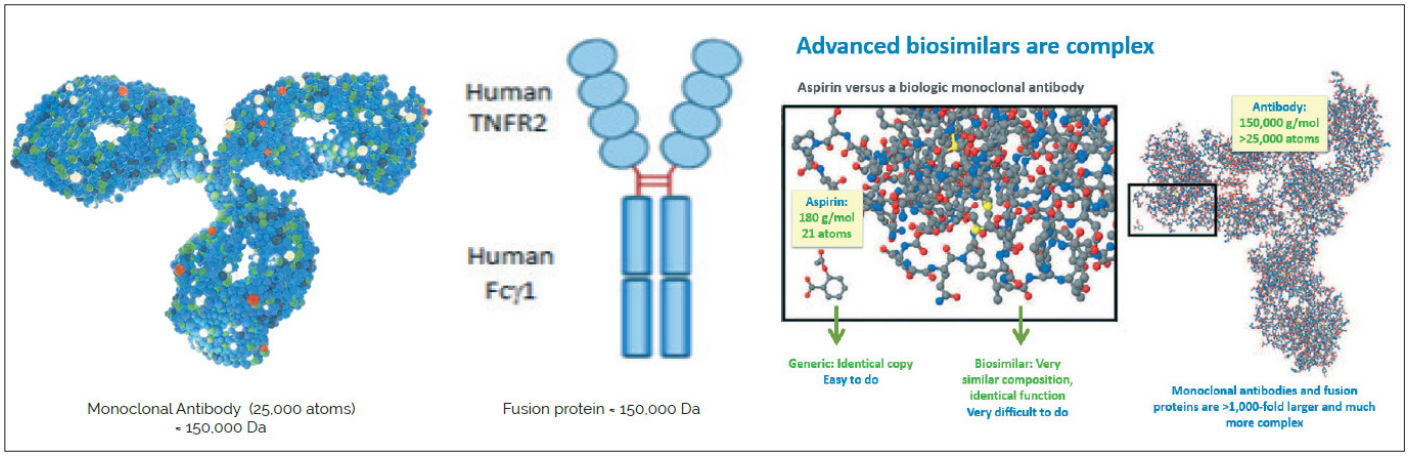
Introduction

Biologics are the drugs whose active substance is produced or excreted from the biological sources - human, animal or microbiological.

Advanced biologics are highly complex molecules.

Development and production are very demanding - manufactured in carefully supervised and monitored conditions (including the many steps necessary to obtain a consistent product).

Biologic Drugs are: vaccines, insulin, fusion receptors, hormon growth, erythropoetin, monoclonal antibodies [1].



Biosimilars are biologic drugs highly similar to another EU-approved biological drugs (so-called "reference drugs").

They are approved according to the same pharmaceutical quality, safety and efficacy standards that apply to all EU-approved biologics.

Since biosimilars are produced in living organisms, there may be fewer differences in comparation with reference drugs.

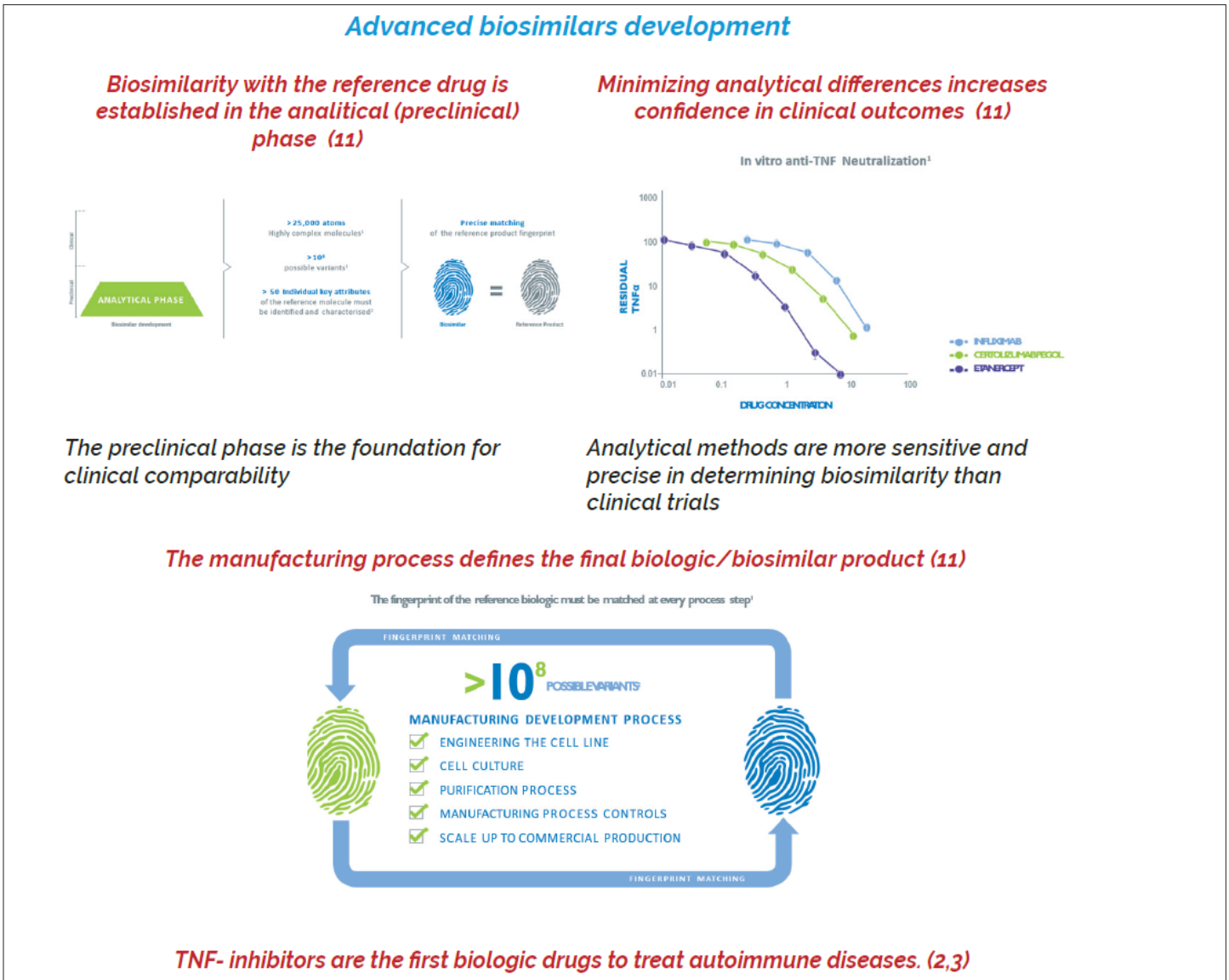
Natural variability is inherent to all biological drugs and strict controls are always present to ensure that it does not affect the way the medicine works or its safety [1,2].

Objectives

Presenting company Ewopharma as a most valuable partner in marketing biosimilars in immunology therapeutic area.
In this research, there are certain findings regarding the following topics:

1. What biological drugs are and whether there is a difference between the original biologic and biosimilar.
2. If applicable, is it relevant and refers to clinical efficacy and safety in treatment of autoimmune diseases.
3. What is the mechanism of action of biological drugs in the treatment of autoimmune diseases.
4. Advantages and disadvantages of biologics introduction in these groups of patients.

Results



Drug	Structure	Target molecule	Route of adm.	Dose	Frequency of application
infliximab	chimeric antibody (human mouse)	TNF-α	iv.	5 mg/kg	Week 0,2 i 6 then every 8 weeks
adalimumab	human antibody	TNF-α	sc.	40 mg	every 2 weeks
etanercept	human recombinant receptor / Fc fusion	TNF-α and llmfotoksl n- α	sc.	50 mg	weekly
certolozumab-per-gol	Fab fragment of humanized antibody bound to PEG	TNF-α	sc.	400 mg	400 mg week 0,2,4 then every 4 weeks 400 mg
golimumab	human antibody	TNF-α	sc.	50 mg	monthly

Mechanism of action (MoA): The immune response suppression mediated by cytokines (Th1 cells) causes a decrease in disease activity [3].

TNF-α inhibitors are: adalimumab, etanercept, infliximab, golimumab, certolizumabpergol.

Indications: RA, JIA, AS, axSpA, PsA, UC, CD, Pso, HS, uveitis, dactylitis and enthesitis [4,5].

Treatment Algorithm

EULAR Recommendations: TNF-α inhibitors are indicated for the treatment of autoimmune diseases after inadequate response to at least one conventional synthetic drug [6].

GRAPPA guidelines provide the possibility of introducing TNF-α inhibitors earlier.

By introducing TNF-α inhibitors in therapy, cl.studies and cl.practice data showed that CR (ACR 20) was not achieved in 40% of patients, suggesting the need for new therapeutic options.

In the Case of TNF-α Inhibitors Ineffectiveness, there is a Possibility of Switching to

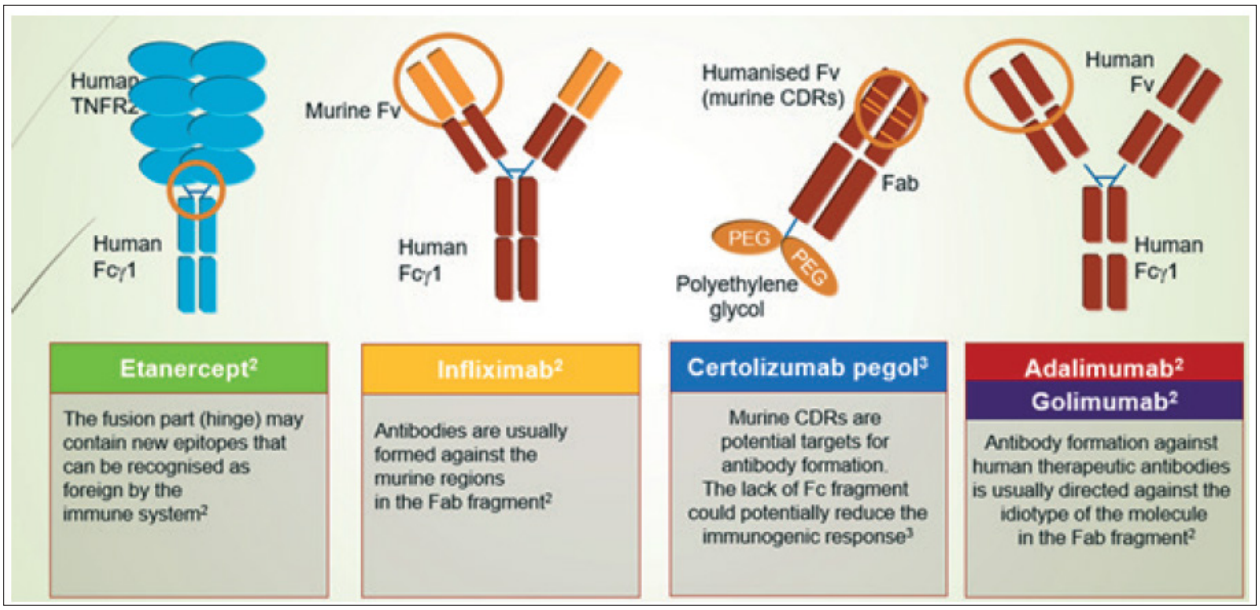
1. Another drug from the group
2. Biological drug with different mechanism of action (interleukin inhibitors) or to
3. Phosphodiesterase blocker or other synthetic (chemical) drug with new MoA (apremilast, tofacitinib, barecitinib)

Switching to the biologic drug with different MoA is superior in comparation with the switching to the drug within the same group [6].

Biologics Effect

Positive: new targeted drugs, effectiveness, rare drug interactions, usage during pregnancy.
Negative: serious side effects, IV or SQ application, price, immunogenicity [7,8].

Part of Molecules which Could Cause Immunogenicity [8]



Interleukin inhibitors are another group of biological drugs with a different mechanism of action in comparation with TNF- inhibitors.

MoA: Human monoclonal antibodies that bind and neutralize (with high affinity) interleukin receptors.

Relatively safe medicines, their toxicity profile is similar to the profile of TNF-α inhibitors and other biologic drugs.

Their usage is advised as an alternative to TNF-α inhibitors in the case of their contraindications, intolerance or inefficiency [2].

Interleukin Inhibitors Include

Daclizumab (inh. IL-2 receptor T-cells, MS treatment), Canakinumab (inh.IL-1 receptor, CAPS syndrome treatment), Brodalumab (inh. IL-receptor, plaque psoriasis treatment), Sarilumab (inh. IL-6 receptor, RA treatment), Ustekinumab (inh.IL-12 and 23 receptor, PsA, psoriasis and CD treatment), Secukinumab (inh.IL-17A, SpA, PsA and psoriasis treatment), Iksekizumab (inh.IL-17A, plaque psoriasis treatment) [2].

Conclusion

There is no significant difference between biologics and their biosimilar drugs refering to cl.efficacy and safety.

Process of manufacturing could influence quality and efficacy of final biologic product (variety in manufacturing process and development of biologics and biosimilars).

The development of targeted therapy has made great progress in the treatment of all autoimmune diseases.

Despite a significant step forward, which means the introduction of TNF-α inhibitors in treating autoimmune diseases, we became aware that 40% of patients did not achieve the minimum level of therapeutic response (given by ACR20).

Therefore, the introduction of more targeted drugs over the last few years is another important step forward, which means a therapeutic alternative to patients with insufficient response to TNF-α or their intolerance [6,9].

Physicians should be careful in introducing it to patients since

cl.efficacy and safety is shown in randomised cl.studies rather than in clinical practice.

It is necessery to provide efficacy and safety treatment follow-up in way to monitor pharmacovigilance and patients registers worldwide.

Discussion on estimating cost-effectiveness (when deciding on drug choice) has been re-evaluated [10-12].

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