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Clinical Outcomes Associated with Switching from Biologics to Biosimilars

An increasing number of biosimilar products are entering the pharmaceutical market. Biosimilars are biological molecules that are copies of existing licensed biologicals in which there are no clinically meaningful differences in safety, efficacy, and immunogenicity compared to the reference medication. Although no safety or efficacy concerns have been observed over the 10 years and greater than 700 million days of patient experience with biosimilars, there have been concerns that switching between these medications may lead to a loss of safety or efficacy. This issue of *CLIPs* briefly summarizes an article that evaluates the clinical outcomes associated with switching from reference medications to biosimilars. If you need further information, please contact the Center for Healthcare Innovation and Patient Outcomes Research (CHIPOR) at chipor@samford.edu.

Cohen HP, Blauvelt A, Rifkin RM, Danese S, Gokhale SB, Woollett G. Switching reference medicines to biosimilars: a systematic literature review of clinical outcomes. Drugs. 2018;78:463-478.

Introduction

- Biological medicines are made up of living systems.
- In order for a biosimilar to be approved for use, no clinical meaningful differences in safety, efficacy, and immunogenicity is observed when directly compared with the reference medication.
- Immunogenicity is typically detected by anti-drug antibody (ADA) assays and neutralizing antibodies (NAB) assays are helpful to determine the potential for clinical relevance of the ADAs.

Methods

- A systematic search in Medline and Embase was conducted for studies published prior to June 30, 2017.
- MeSH terms used included “biosimilar pharmaceuticals” OR “biologic factors”.
- Additional search terms were added including: erythropoietin; human growth hormone; filgrastim; etanercept; adalimumab; infliximab; rituximab; and drug substitution.
- Non-English, non-human studies and editorials were excluded from the review.
- The investigators evaluated the degree, if at all, differences in switching from biologic reference medications to biosimilars would alter clinical outcomes.

Results

- A total of 2,045 citations were located and 151 articles were selected for the systematic review.
- The products were divided into their respective sizes: smaller proteins (n=57 studies) and larger proteins (n=94 studies).
- A total of 90 studies, containing both smaller and larger proteins were included.
- The studies included 7 different products that covered 14 diseases.
- The majority of the studies included 30-60 patients; however, 33 studies enrolled more than 100 subjects each. Eight studies enrolled fewer than 20 patients.
- Most of the studies were pharmacokinetic / pharmacodynamics in nature.
- A total of 36 publications described efficacy of primary data.
- Overall efficacy was similar between the reference and biosimilar product.
- Several studies focused on safety endpoints of the larger biologics. Treatment emergent adverse events (TEAEs) were reported in 39 studies.
- TEAEs were similar across disease indications.

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Arthritis studies

- Several arthritis studies were evaluated and outcomes included disease activity scores and ACR 20/50/70 measures (20%, 50%, or 70% response from the American College of Rheumatology questionnaire's measure of improvement in tendor or swollen joints).
- No clinically significant differences in safety and efficacy of the infliximab biosimilar, CT-P13, study were observed.
- SB2 molecule was evaluated in a randomized, double-blinded, parallel group study compared to infliximab for paients with moderate-to-severe rheumatoid arthritis (RA). No changes in efficacy or safety were noted.

Inflammatory bowel disease studies

- Efficacy measures included disease activity indices.
- Infliximab biosimilar was compared to the reference and outcomes were comparable between the biosimilar and infliximab.

Psoriasis studies

- Five psoriasis articles were included that assessed psoriasis area severity index (PASI) and visual analogue scale (VAS).
- Etanercept and adlimumab biosimlars were evaluated against their respective reference medications.
- No clinically significant differences were noted between the comparable and references.

Hematology-Oncology studies

- A total of 19 studies were included for the following products: filgrastim, human growth hormone, and erythropoietin. The most common indication was chronic kidney disease (CKD).
- Efficacy was comparable in all erythropoietin studies (e.g., stable mean Hb levels in end stage renal disease studies).
- Filgrastim studies, that included multiple switches, were associated with similar outcomes between the reference agent and biosimlar.
- Human growth hormone studies yielded similar outcomes between the studies.

Discussion

- Most studies indicated that there is no differences in clinical outcomes between the reference and biologic product.
- No loss of effiacay was observed and no new adverse effects were detected.
- The review is limited by the high variability of methods used by individual investigators.
- Some information was obtained from abstracts only and this may not have provided much detail about the clinical study.
- The quality of the studies were not evaluated.

Summary

- A total of 17 disease indications were evaluated in 14,225 patients.
- No clinicallly significant changes in clinical impact were noted between reference agents and biosimilars.

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