LETTER TO THE EDITOR

Biosimilars in Crohn’s disease

The patent for some biological medicines used in the treatment of Crohn’s disease are close to expire. Biosimilars are biologicals sufficiently similar to a biopharmaceutical already approved by a regulatory agency.1 Several companies are developing biosimilars to tumor necrosis factor and the first biosimilar submitted to the European agency for the treatment of rheumatoid arthritis was developed in Korea by Celltrion and was approved by regulators. The review concluded that the biosimilar named Inflectra has demonstrated similar quality efficacy and safety to Remicade. Their commendation was not only for its use in rheumatoid arthritis but also for the extrapolation for indication in other forms of inflammatory arthritis.2 Surprise as it may be extrapolation was also extended to Crohn’s disease (CD).

There is plenty of evidence for the role of TNF on the chronicity of the mucosal inflammation in CD but the cytokine network associated with the immunopathogenesis of the disease is different from what one observes in inflammatory arthritis. The metrics of improvement are also quite distinct when one considers the evaluation of tenderness and swelling of joints and migrates to diarrhea fistulas and abdominal pain. No patient with CD responds or maintains a response to anti-tumor necrosis factor (TNF) agents in a frequency considerably higher than what is observed in rheumatoid arthritis and alternative treatments are necessary. Natalizumab, a monoclonal antibody to alpha-4 integrin approved for CD, has demonstrated efficacy in randomized clinical trials in bowel disease but no effect on arthritis was observed. Immunogenicity of infliximab in patients with CD appears to occur substantially more frequently than in patients with inflammatory arthritis. New biologics are in development for CD such as interferon gamma and GM-CSF that have no therapy activity in inflammatory arthritis.3 While abbreviated pathway of approval will impact the final price of a biosimilar we feel that extrapolation to inflammatory bowel disease without a comparative trial is a controversial decision that may not have all the immunopathogenetic rational that one would expect in taking care of such patients. In fact, the recent position from ECCO emphasizes that clinical efficacy of a biosimilar in inflammatory arthritis should not be extrapolated for IBD where efficacy cannot be predicted by effectiveness for other indications.4 In conclusion, while anti-TNFs offer a distinct advantage in the treatment of CD since it is a target therapy other immunoinflammatory mechanisms are also playing a role such as other cytokines and integrins. We suspect that gastroenterologists similar to what is known for rheumatologists are still not well familiarized with the challenges and concerns in the development of biosimilars.5 However, our opinion is that comparable trials should be performed between the reference biologic and the biosimilar in CD before they get marketing authorization for use in clinical practice.

Disclosures

None.

References


Morton Scheinberg
Division of Clinical Research, Hospital da AACD, São Paulo, Brazil
Hospital Albert Einstein, São Paulo, Brazil
E-mail address: morton@osite.com.br.

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