DOI: 10.1590/S0004-28032016000200002 ARQGA/1829

ANVISA APPROVES THE FIRST BIOSIMILAR MONOCLONAL ANTIBODY BASED ON COMPARABILITY IN BRAZIL

Fábio Vieira **TEIXEIRA**, Paulo Gustavo **KOTZE** and Adérson Omar Mourão Cintra **DAMIÃO**

Received 14/2/2016
Accepted 1/3/2016

Teixeira FV, Kotze PG, Damião AOMC. ANVISA approves the first biosimilar monoclonal antibody based on comparability in Brazil.
HEADINGS - Biosimilar pharmaceuticals. Crohn disease. Ulcerative colitis.

Dear Sir,

On April 27th, 2015, the National Health Surveillance Agency of Brazil (ANVISA) approved the first biosimilar monoclonal antibody in Brazil. CT-P13 is produced by a South Korean pharmaceutical company and will be marketed and distributed in Brazil by a partnership between two American companies[1,18,19].

CT-P13 is a biosimilar medication to Infliximab (IFX), which uses the original product, manufactured in the United States as the reference drug[1,2,3,6,18,19]. This measure by ANVISA is primarily aimed at cost reduction, because most of the individuals currently using IFX can only do it due to reimbursement by the Brazilian public health system. The achievement is commendable and approved by all medical societies involved, in the specialties of rheumatology, gastroenterology and dermatology. However, scientific, safety and pharmacovigilance issues have arisen and should be carefully addressed and widely discussed within this new scenario for the benefit of patients. CT-P13 has been approved in Brazil based on comparability strictly following the regulations of ANVISA[1,18,19]. The original IFX was approved in Brazil in 2000 for the treatment of luminal Crohn´s disease. This drug is also approved in our country in other indications: rheumatoid arthritis, psoriasis, ankylosing spondylitis, psoriatic arthritis, fistulizing Crohn's disease and ulcerative colitis. In accordance with the European Agency (EMA - European Medicine Agency), ANVISA also follows strict international standards for the approval of biosimilar agents[1,2,3,6,9,18,19]. As mentioned, CT-P13 has been approved by ANVISA based on comparability. To be approved by the Brazilian agency, the drug has been successfully tested in humans in two clinical studies in rheumatology patients: a phase I clinical study in ankylosing spondylitis and a phase III study in patients with rheumatoid arthritis[15,20]. The use of CT-P13 for other diseases listed in the reference drug package insert was approved based on the concept of extrapolation of indications[1,18,19].

In October 2014 the Biosimilar commission of the Brazilian Study Group of Inflammatory Bowel Diseases (GEDIIB) submitted to ANVISA an opinion contrary to the approval of CT-P13 for patients with inflammatory bowel diseases (IBD)[6]. Recently, the Brazilian Societies of Rheumatology, Dermatology and Gastroenterology (represented by GEDIIB) issued the same position[2]. Exactly in accordance with the opinion of Health Canada, the local Canadian agency responsible for the medication control in that country, the position issued by GEDIIB made it clear that although the biosimilar is a positive and welcome evolution in the IBD setting, it would be essential to carry out clinical studies with biosimilar products in a specific population with IBD patients. Indeed, these studies could elucidate the controversial points regarding the efficacy and safety of the long-term use of this biosimilar drug[4].

A small number of cases of IBD patients treated with CT-P13 have been published to date[5,7,8,10-12,17,21]. Moreover, it is also known that there is still no prospective head-to-head or non-inferiority randomized studies comparing CT-P13 with the reference IFX. On the other hand, after the product has been used for more than 2 years in eastern Europe and Korea, post-marketing studies presented at scientific meetings have described good results regarding the efficacy and safety of CT-P13 both in

This article did not have any founding source
Study carried out at Grupo de Estudos da Doença Inflamatória Intestinal do Brasil - GEDIIB.
Biosimilars Committee of Grupo de Estudos da Doença Inflamatória Intestinal do Brasil - GEDIIB (Brazilian Study Group of Inflammatory Bowel Diseases) and Federação Brasileira de Gastroenterologia - FBG (Brazilian Federation of Gastroenterology).
Correspondence: Prof. Dr. Fábio Vieira Teixeira. Avenida São Paulo, 62. Bairro Cascata - CEP 17509-190 - Marília, SP, Brasil. E-mail: fabio@gastrosaude.com

the adult and pediatric population with IBD[5,7,8,10-13,17,21]. However, a retrospective study conducted in Ireland using a controversial methodology showed a significant increase in hospitalizations, use of corticosteroids and surgery in patients treated with CT-P13, as compared to those who received the reference drug IFX[14]. As this is, to date, the only study showing discrepancies in efficacy and safety between the biosimilar and the reference drug, it is vital that we carefully analyze these results and that we remain alert and vigilant.

For sure more publications with biosimliars in the IBD scenario will arise in the years to come. Special attention to these new data must be given. The spread use of biosimilars is a question of time, as an important economic impact will benefit stakeholders. Consequently, the number of patients treated with monoclonal antibodies will increase over the years.

Authors' contributions

Teixeira FV, Kotze PG and Damião AOMC drafted the article and gave final revision.

Disclosure

Teixeira FV, Kotze PG and Damião AOMC are speakers and consultants for Abbvie and Janssen. FVT is a speaker and consultant for Hospira. Kotze PG and Damião AOMC are speakers and consultants for Takeda. Damião AOMC is an employee for Nestle.

Teixeira FV, Kotze PG, Damião AOMC. Aprovação pela ANVISA do primeiro anticorpo monoclonal biosimilar baseada em comparabilidade no Brasil. Arq Gastroenterol. 2016,53(2): 60-1.

DESCRITORES - Medicamentos biossimilares. Doença de Crohn. Colite ulcerativa.

REFERENCES

1. ANVISA. Primeiro medicamento biológico por comparabilidade é aprovado pela ANVISA. [Internet]. [Accessed 2015 Ap 27]. Available from: http://s.anvisa.gov.br/wps/s/r/dhM6
2. Azevedo VF, de Souza Meirelles E, Kochen JA, Medeiros AC, Miszputen SJ, Teixeira FV, Damião AO, Kotze PG, Romiti R, Arnone M, Magalhães RF, Maia CP, de Carvalho AV. Recommendations on the Use of Biosimilars by the Brazilian Society of Rheumatology, Brazilian Society of Dermatology Brazilian Fed eration of Gastroenterology and Brazilian Study Group on Inflammatory Bowel Disease - Focus on Clinical Evaluation of Monoclonal Antibodies and Fusion Proteins Used in the Treatment of Autoimmune Diseases. Autoimmun Rev. 2015;14:769-73.
3. Beck A, Reichert JM. Approval of the first biosimilar antibodies in Europe: a major landmark for the biopharmaceutical industry. MAbs. 2013;5:621-3.
4. Canadá. Health Products and Food Branch, Health Canada. Guidance for sponsors: information and submission requirements for subsequent entry biologics (SEBs). 2010. [Internet]. [Accessed 2014 Sept 10]. Available from: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/brgtherap/applic-demande/guides/seb-pbu/seb-pbu-2010-eng.pdf
5. Gecse KB, Lovász BD, Farkas K, Banai J, Bene L, Gasztonyi B, et al. Efficacy and safety of the biosimilar infliximab CT-P13 treatment in inflammatory bowel diseases: a prospective, multicentre, nationwide cohort. J Crohns Colitis. 2016;10:133-40.
6. Grupo de Estudos da Doença Inflamatória Intestinal (GEDIIB). Relatório do Grupo de Estudos da Doença Inflamatória Intestinal para ANVISA com respeito ao uso de biossimilar na DII. [Internet]. [Accessed 2015 Feb 2]. Available from: http://gediib.org.br/?noticias&dado_id=252
7. Jarzebicka D, Banaszkiewicz A, Plocek A, Sieczkowska J, Gawronska A, Toporowska-Kowalska, Kierkus J. Preliminary assessment of efficacy and safety of switching between originator and biosimilar infliximab in paediatric Crohn disease patients. J Crohn's Colitis. 2015;9:S224-5.
8. Jarzebicka D, Plocek A, Sieczkowska J, Toporowska-Kowalska E, Kierkus J. First observations of the use of biosimilar infliximab for treatment of ulcerative colitis in paediatric population. J Crohn's Colitis. 2015;9:S307-S8.
9. Jung SK, Lee KH, Jeon JW, Lee JW, Kwon BO, Kim YJ, Bae JS, Kim DI, Lee SY, Chang SJ. Physicochemical characterization of Remsima®. MAbs. 2014;6:1163-77.
10. Jung YS, Park DI, Kim YH, Lee JH, Seo PJ, Cheon JH, Kang HW, Kim JW. Efficacy and safety of CT-P13, a biosimilar of infliximab, in patients with inflammatory bowel disease: A retrospective multicenter study. J Gastroenterol Hepatol. 2015;30:1705-12.
11. Kang HW, Lim YJ, Kim JH, Kang Y. An experience of anti-TNF biosimilar, CT-P13 use: clinical efficacy, safety and interchangeability in inflammatory bowel disease; a pilot study. J Crohn's Colitis. 2014;8:S303.
12. Kang YS, Moon HH, Lee SE, Lim YJ, Kang HW. Clinical Experience of the Use of CT-P13, a Biosimilar to Infliximab in Patients with Inflammatory Bowel Disease: A Case Series. Dig Dis Sci. 2015;60:951-6.
13. Molnar T, Farkas K, Rutka M, Bálint A, Nagy F, Bor R, Milassin Á, Szepes Z. Efficacy of the new infliximab biomarker CTP13 induction therapy on mucosal healing in ulcerative colitis patients. J Crohn's Colitis. 2015;9:S382.
14. Murphy C. Sugrue K, Mohamad, McCarthy J, Buckley M. Biosimilar but not the same. J Crohn's Colitis. 2015;9:S331-2.
15. Park W, Hrycaj P, Jeka S et al. A randomized, double-blind, multicentre, parallel-group, prospective study comparing the pharmacokinetics, safety, and efficacy of CT-P13 and innovator infliximab in patients with ankylosing spondylitis: the PLANETAS study. Ann Rheum Dis. 2013;72:1605-12.
16. Reichert JM. Next generation and biosimilar monoclonal antibodies: essential considerations towards regulatory acceptance in Europe. February 3-4, 2011, Freiburg, Germany. MAbs 2011;3:223-40.
17. Sieczkowska J, Banaszkiewicz A, Plocek A, Jarzebicka D, Gawronska A, Toporowska-Kowalska E, Kierkus J. Assessment of safety and efficacy of biosimilar infliximab in children with Crohn disease: a preliminary report. J Crohn's Colitis. 2015;9:S295.
18. Teixeira FV, Kotze PG, Damião AOMC, Miszputen SJ. Biosimilars in inflammatory bowel diseases: an important moment for Brazilian Gastroenterologists. Arq Gastroenterol 2015;52:76-80.
19. Teixeira FV. First biosimilar of infliximab approved in Brazil: response from the Brazilian IBD society. GaBI Journal. 2016;5:1-2. Available from: www.gabi-journal.net
20. Yoo DH, Hrycaj P, Miranda P, et al. A randomized, double-blind, parallel-group study to demonstrate equivalence in efficacy and safety of CT-P13 compared with innovator infliximab when co administered with methotrexate in patients with active rheumatoid arthritis: the PLANETRA study. Ann Rheum Dis. 2013;72:1613-20.
21. Yoon Suk J, Park DI, Kim YH, Seo PJ, Kim JW, Kang HW. Efficacy and safety of infliximab's biosimilar (REMSIMA®) for IBD. J Crohn's Colitis. 2015;9:S349-50.