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Biosimilar knowledge and viewpoints among Brazilian inflammatory bowel disease patients

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Abstract

Background: In this analysis we aimed to describe Brazilian inflammatory bowel disease (IBD) patients' knowledge and perceptions regarding biosimilars and compare with viewpoints from non-Brazilian patients.

Methods: An online survey consisting of 19 questions was made available by the European Federation of Crohn's and Ulcerative Colitis Associations between July 2018 and December 2018. Only respondents who had heard of biosimilars were asked to respond to all of the questions.

Results: A total of 102 Brazilian IBD patients responded to the survey. The majority (78.4%) of patients had been exposed to anti-tumor-necrosis-factor drugs and 63.4% of them had heard of biosimilars. Brazilian respondents worried significantly more about biosimilars being less effective than the originator (62.5% *versus* 47.9%, *p* value 0.03) and molecular differences between biosimilars and originators (53.1% *versus* 31.8, *p* value 0.001) as compared with non-Brazilian IBD patients. The majority of Brazilian (75%) and non-Brazilian (64.1%) respondents thought that the lower cost of biosimilars should not come before their safety and efficacy (*p* value 0.09). In addition, 79.1% of Brazilian respondents believed that the arrival of biosimilars will have an impact on the management of IBD.

Conclusions: Brazilian patients reported higher rates of misconceptions regarding biosimilars than non-Brazilian IBD patients. Although patients still worry about different aspects regarding biosimilars, they also tend to be confident that biosimilars will have an impact on the management of their disease. With the recent approval of many biosimilars in Brazil and the imminent widespread use of these drugs, our data raise awareness for the need of providing patient education to prevent negative expectations toward switching to biosimilars.

Keywords: adalimumab, biosimilar, inflammatory bowel disease, infliximab

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Introduction

Biological therapy has become the mainstay of treatment of inflammatory bowel disease (IBD) over the past 20 years.[1] The wide adoption of biologics in IBD care has led to an exponential increase in treatment-related costs. In this context, biosimilars, less expensive drugs, have been developed aiming greater access to biologic therapies.[2,3]

The European Medicines Agency (EMA) defines biosimilar as biological medicine highly similar to another already approved biological medicine (the 'reference medicine'), with no clinically meaningful differences among them.[4] The regulatory process required for the market authorization of biosimilars relies mainly on the comparability exercise *versus* the reference product, but also includes the analysis of pharmacokinetic,

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pharmacodynamic, and efficacy studies. These drugs in general cost less than the original drugs, but they can only be marketed after data patent protection has expired.[5]

Biosimilar uptake has greatly increased in Europe over the last few years, and many observational data have reassured safety and efficacy of these drugs in IBD.[5] However, experience with biosimilars in Brazil is still limited given the recent introduction of these drugs in the country. CT-P13, the first biosimilar approved for Crohn's disease (CD) and ulcerative colitis (UC) was recently launched (2013 in Europe and 2015 in Brazil). In Brazil, biosimilars approved for IBD are CT-P13 (REMSIMA®), from the infliximab reference (REMICADE®, Janssen), and the adalimumab biosimilar (AMGEVITA® and HIRIMOZ®), from the adalimumab reference (HUMIRA®, Abbvie).[6,7]

Patients may have different perceptions toward these recently introduced drugs, which can create barriers to their uptake.[8] Moreover, improved patient understanding on the rationale for initiating or switching to biosimilars may encourage greater acceptance of biosimilars.[9] Therefore, the purpose of this study was to analyze the perception and knowledge from Brazilian IBD patients regarding biosimilars, through the sub-analysis of a European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) web-based survey and highlight the main differences between the perceptions of biosimilars among Brazilian and non-Brazilian IBD patients.

Materials and methods

The questionnaire

The questionnaire was developed by the EFCCA in collaboration with IBD experts in the field, and it consisted of 19 questions. It was carried out as an online survey, available from July to December 2018 on the EFCCA website, and offered in another seven languages apart from English, including Portuguese. The national member associations of EFCCA were responsible for informing their membership about the survey. After basic demographic questions, only those respondents who had heard of biosimilars continued to the biosimilar-specific questions.

The participants

The participants of the survey were members of EFCCA associations or people following the communications of these associations.

Ethical consideration

The recruitment was self-selective, dispensing the requirement for consent form. In addition, data were de-identified and individual participant data were not published, which maintained confidentiality in all steps of study analysis. This study was conducted in compliance with regulations stated in the 1975 Declaration of Helsinki.

Statistical considerations

The response variables were categorical. Explanatory variables were integer age and binary disease. A binary logit model was used for the response variables that had only two possible values and a generalized logit model for the variables that had more than two possible values. In some questions, some observations were deleted as a result of missing values for the response or explanatory values. Students' t test and chi-square were used to analyze the data, accordingly. A two-tailed p value of 0.05 was used for statistical significance.

Results

Respondent demographics

A total of 106 Brazilian patients responded to the survey. Out of them, 81.1% ($n=86$) had CD, 15.1% ($n=16$) had UC, 1.9% ($n=2$) had gluten sensitivity, and 1.9% ($n=2$) a rheumatic disease. Only respondents with IBD ($n=102$) were included in the analysis. The respondents (37.5%) were 31–45-years old, and 1.9% had been diagnosed in 1990 or before, 6.7% between 1991 and 2000, 29.8% between 2001 and 2010, and 60.6% in 2010 or later (Table 1).

Exposure to biologics and biosimilars

Regarding current and previous exposure to anti-tumor-necrosis-factor (anti-TNF) therapy, 67.6% of Brazilian IBD patients were currently being treated with anti-TNF; 4.9% had been treated with anti-TNF in the past, but the therapy

Table 1. Demographic characteristics of Brazilian and non-Brazilian respondents.

	Brazilian IBD patients		Non-Brazilian IBD patients		*p* value
	Mean	**Standard deviation**	**Mean**	**Standard deviation**	
	***n* = 102**		***n* = 1516**		
Age at the time of research (years)	34	13	41	14	<0.05
	***n* = 101**		***n* = 1505**		
Age at the time of IBD diagnosis (years)	26	11	29	12	0.11
	Median		**Median**		
Year at the time of IBD diagnosis	2013		2008		<0.05
IBD diagnosis	***n* = 102**		***n* = 1517**		
	***n* (%)**		***n* (%)**		
	Ulcerative colitis	**Crohn's disease**	**Ulcerative colitis**	**Crohn's disease**	
	16 (15.7)	86 (84.3)	589 (38.8)	928 (61.2)	<0.05

IBD, inflammatory bowel disease.

had been discontinued due to inefficacy, and 5.9% had received anti-TNF in the past, but the therapy was discontinued due to side effects. Only those patients who had heard of biosimilars (63.4%) continued to the biosimilar-specific questions (Table 2).

Concerns about biosimilars

In reference to general aspects of biosimilars, Brazilian respondents were more likely to express concerns regarding the efficacy of biosimilars (62.5% *versus* 47.9%, *p* value 0.03) and molecular differences between biosimilars and originators (53.1% *versus* 31.8, *p* value 0.001) as compared with non-Brazilian IBD patients. Only 12.5% of Brazilian respondents had no specific concerns about biosimilars (Table 2).

Lower price of biosimilars

Most Brazilian IBD patients (53.1%) believed that cost sparing provided by biosimilars will expand access to biologic agents to more patients, which is in line with the conceptions of non-Brazilian IBD patients (48.1%, *p* value 0.5). In addition, 75.0% of Brazilian and 64.1% of non-Brazilian patients think cost savings should not come before the efficacy and safety of the treatment (*p* value 0.09). The vast majority (92.2%) of patients believed that this savings will not impact economic status and 6.2% believe that it will not make any difference to the economy (Table 2).

Extrapolating data

The respondents were told that the biosimilar of Remicade® was approved for the treatment of IBD by extrapolating data from rheumatoid arthritis and were asked how they felt about this. The majority of Brazilian IBD patients (57.8%) would prefer if it could be tested for inflammatory bowel diseases before extrapolating the data from rheumatologic disorders, while 51.6% would wait for more data in IBD before accepting a biosimilar for either CD or UC, as compared with 31.2% (*p* value 0.05) of non-Brazilian IBD patients. Just 6.2% of the Brazilian respondents would trust the decisions made by regulatory agencies and would not wait for IBD-specific data. Moreover, 34.4% of the Brazilian respondents would trust their treating physician, who would make the decision to use biosimilars in their treatment and just 7.8% would trust their pharmacist to make the decision to use biosimilars in their treatment (Table 2).

Table 2. Results of questions 1–15 and comparison with non-Brazilian IBD patients.

Question 1		**Brazilian IBD patients**	**Non-Brazilian IBD patients**	***p* value**
		***n* = 102**	***n* = 1220**	
		***n* (%)**	***n* (%)**	
Exposure to anti-TNF therapy (infliximab (Remicade), adalimumab (Humira), certolizumab (Cimzia), golimumab (Simponi)	(a) Currently treated with anti-TNF	69 (67.6)	607 (49.8)	<0.05
	(b) Received anti-TNF in the past, therapy discontinued due to inefficacy	5 (4.9)	103 (8.4)	
	(c) Received anti-TNF in the past, therapy discontinued due to side effects	6 (5.9)	98 (8.0)	
Question 2		***n* = 63**	***n* = 1157**	
Have you been previously or are you currently being treated with an infliximab biosimilar (Inflectra, Remsima or Flixabi)?	Yes	9 (14.3)	221 (19.1)	0.40
Question 3		***n* = 101**	***n* = 1253**	
Have you ever heard of biosimilars?	Yes	64 (63.4)	532 (42.5)	<0.05
Question 4		***n* = 64**	***n* = 541**	
		***n* (%)**	***n* (%)**	
Concerning biosimilars, you worry (it is possible to choose more than one option):	(a) That the molecular basis of the biosimilar is different from that of the reference drug	34 (53.1)	172 (31.8)	<0.05
	(b) About safety profile (mainly infections and cancers)	29 (45.3)	246 (45.5)	1.00
	(c) About tolerability	26 (40.6)	156 (28.8)	0.06
	(d) That the biosimilar could be less effective than the reference drug	40 (62.5)	259 (47.9)	<0.05
	(e) You don't know	8 (12.5)	123 (22.7)	0.08
Question 5		***n* = 64**	***n* = 541**	
		***n* (%)**	***n* (%)**	
The biosimilar will be less expensive than the reference drug, you think that (it is possible to choose more than one option):	(a) This is good news because more patients will be treated with biologics	34 (53.1)	260 (48.1)	0.50
	(b) The cost of a treatment should not come before its effectiveness or safety/tolerance	48 (75.0)	347 (64.1)	0.09
	(c) This will help cost savings	5 (7.8)	126 (23.3)	<0.05
	(d) You don't think that a lower cost will change something	4 (6.2)	48 (8.9)	0.60

(continued)

Table 2. (Continued)

Question 1		Brazilian IBD patients	Non-Brazilian IBD patients	*p* value
		n = 102	*n* = 1220	
		n (%)	*n* (%)	
Question 6		***n* = 64**	***n* = 541**	
The biosimilar of Remicade (infliximab) has been successfully developed and used for the treatment of rheumatologic diseases. On June 27 2013, the biosimilar of Remicade (infliximab) received positive opinion from the European Medicines Agency (EMA) for the treatment of IBD by extrapolating data from rheumatoid arthritis (it is possible to choose more than one option):	(a) You think that it makes sense, because its efficacy and safety profile has been established for other chronic conditions than IBD	14 (21.9)	112 (20.7)	0.87
	(b) You would prefer if it could be tested for inflammatory bowel diseases before extrapolating data from rheumatologic disorders	37 (57.8)	299 (55.3)	0.79
	(c) You trust the decisions made by regulatory agencies and you are not awaiting data in IBD	4 (6.2)	52 (9.6)	0.49
	(d) You trust your treating physician who will make the decision to use biosimilars in your treatment	22 (34.4)	246 (45.5)	0.11
	(e) You trust your pharmacist to make the decision to use biosimilars in your treatment	5 (7.8)	9 (1.7)	<0.05
	(f) You are waiting for more data in IBD before accepting a biosimilar for either Crohn's disease or ulcerative colitis	33 (51.6)	169 (31.2)	<0.05
Question 7		***n* = 64**	***n* = 541**	
Now that biosimilars are coming to the market, you think (it is possible to choose more than one option):	(a) That patient associations should be informed and should be able to give their opinion	42 (65.6)	330 (61.0)	0.50
	(b) That patients should systematically be given information	50 (78.1)	417 (77.1)	1.00
	(c) That we should wait for many patients to receive biosimilars in a real-life setting before recommending its use in a large population of IBD patients	29 (45.3)	225 (41.6)	0.59
	(d) We should know in which country the drug has been tested/created before using it in your own country	31 (48.4)	174 (32.2)	<0.05
Question 8		***n* = 63**	***n* = 526**	
		n (%)	*n* (%)	
In the future, biosimilars could be interchangeable with the reference drug:	(a) You are opposed to this idea if the patient is not aware of this decision but accept if the patient is systematically informed	22 (34.9)	161 (30.6)	0.18
	(b) You might accept this exchange if the drug is delivered by your usual pharmacist	0 (0)	23 (4.4)	
	(c) You accept this exchange if your treating physician gives his approval	17 (27)	179 (34)	
	(d) You accept this exchange if evidence-based-medicine data are available	24 (38.1)	163 (31)	

(continued)

Table 2. (Continued)

Question 1		Brazilian IBD patients	Non-Brazilian IBD patients	*p* value
		n = 102	*n* = 1220	
		n (%)	*n* (%)	
Question 9		***n* = 63**	***n* = 528**	
The biosimilar will have the same pharmacological name as the reference drug, so, when prescribed, there will be no way to distinguish it from the reference drug:	(a) You wish to know if you receive the biosimilar or the reference drug	21 (33.3)	256 (48.5)	<0.05
	(b) You don't mind as long as the biosimilar has the same efficacy and safety profile as the reference drug	6 (9.5)	60 (11.4)	
	(c) You would like to be informed about it, but you trust the pharmacist if he delivers it or your treating physician if he prescribes it	9 (14.3)	81 (15.3)	
	(d) You wish to have all the necessary information before the drug is administered and obtain written information (e.g. card) to be used for future care	27 (42.9)	131 (24.8)	
Question 10		***n* = 64**	***n* = 494**	
Do you think that the arrival of biosimilars will have an impact on the management of IBD:	(a) Yes, completely	15 (24.2)	81 (16.4)	0.65
	(b) Probably	28 (45.2)	231 (46.8)	
	(c) Maybe a little	6 (9.7)	58 (11.7)	
	(d) Not at all	3 (4.8)	25 (5.1)	
	(e) Don't know	10 (16.1)	99 (20)	
Question 11		***n* = 62**	***n* = 528**	
		n (%)	*n* (%)	
If a biosimilar is prescribed and explained to you by your treating physician:	(a) You will be fully confident	19 (30.6)	186 (35.2)	0.69
	(b) You will be worried but will accept the treatment	23 (37.1)	197 (37.3)	
	(c) You will probably not accept it and express yourself on this matter	7 (11.3)	65 (12.3)	
	(d) You will ask another physician	7 (11.3)	36 (6.8)	
	(e) You don't know	6 (9.7)	44 (8.3)	

(continued)

Table 2. (Continued)

Question 1		Brazilian IBD patients	Non-Brazilian IBD patients	*p* value
		n = 102	*n* = 1220	
		n (%)	*n* (%)	
Question 12		***n* = 62**	***n* = 526**	
If the pharmacist hands out the biosimilar, changing the initial prescription without the consent of the prescribing physician:	(a) You will accept it because of the lower cost of the biosimilar	0 (0)	21 (4)	<0.05
	(b) You will accept it because of available scientific evidence	5 (8.1)	60 (11.4)	
	(c) You disagree, but you acknowledge that you will have to accept it	6 (9.7)	105 (20)	
	(d) You will try to obtain the reference drug	51 (82.3)	340 (64.6)	
Question 13		***n* = 62**	***n* = 525**	
After starting a treatment with biosimilar:	(a) You will carefully follow the treatment	31 (50)	299 (57)	0.53
	(b) You will be worried and will probably stop the treatment at the first doubt or adverse event	14 (22.6)	97 (18.5)	
	(c) You will be worried, but the fact that the treatment has been approved by the EMA is reassuring	17 (27.4)	129 (24.6)	
Question 14		***n* = 62**	***n* = 528**	
		n (%)	*n* (%)	
You believe that biosimilars (generic: a drug product that is comparable with brand/reference listed drug product in dosage form, strength, route of administration, quality and performance characteristics, and intended use, containing the same active ingredients):	(a) Are like generic drugs	11 (17.7)	142 (26.9)	<0.05
	(b) Are close to generic drugs	8 (12.9)	167 (31.6)	
	(c) Are not at all like generics	31 (50)	118 (22.3)	
	(d) You don't know	12 (19.4)	101 (19.1)	
Question 15		***n* = 62**	***n* = 528**	
Regarding generic treatments: (generic: a drug product that is comparable with brand/reference listed drug product in dosage form, strength, route of administration, quality and performance characteristics, and intended use, containing the same active ingredients):	(a) You take them without concern	23 (37.1)	204 (38.6)	0.61
	(b) You accept them but have some doubts	26 (41.9)	182 (34.5)	
	(c) You refuse them when you can	7 (11.3)	90 (17)	
	(d) You have never thought about this	4 (6.5)	25 (4.7)	
	(e) You don't know	2 (3.2)	27 (5.1)	

IBD, inflammatory bowel disease; TNF, tumor necrosis factor.

Biosimilars coming onto the market

The vast majority of Brazilian IBD patients (78.1%) reported that patients should systematically be given information about biosimilars and 65.6% thought that patient associations should be informed, and able to give their opinion regarding biosimilar issues. Furthermore, 45.3% of the Brazilian respondents thought that many more patients should receive biosimilars in a real-life setting before recommending its use in a large population of IBD patients, and 48.4% thought that the country in which the biosimilar drug had been tested or created should be known before the biosimilar was used in their own country (Table 2).

Interchangeability with reference drug

Respondents were surveyed on their views on interchangeability (Table 2). Among Brazilian respondents, 27.0% would accept the exchange if their treating physician approved it, 38.1% if evidence-based data were available, and 34.9% of the respondents would be opposed to the idea if they were not aware of the exchange. None of them would agree with the drug exchange by the pharmacist. There was no significant statistical difference between Brazilian and non-Brazilian IBD patients on this topic.

Same pharmacological name

When told that the biosimilars would have the same pharmacological name as the reference drug, so that when prescribed, there would be no way to distinguish it from the reference drug, 33.3% of the Brazilian and 48.5% of non-Brazilian respondents said they would want to know whether they were receiving the biosimilar or the reference drug, while 42.9% of the Brazilian and 24.8% of non-Brazilian patients would want to have all the necessary information before the drug was administered, and obtain written information (Table 2).

Biosimilars' impact on the management of IBD

Among Brazilian respondents, 24.2% believed that biosimilars would completely impact the management of IBD, 45.2% believed that the impact would be just probable, 9.7% believed that biosimilars might impact the management of IBD a little and 4.8% of the respondents believed that biosimilars would not impact the management of IBD at all. There was no significant statistical difference between Brazilian and non-Brazilian IBD patients (Table 2).

Biosimilar prescribed and explained by the treating physician

If biosimilars were prescribed and explained by their treating physician, 30.6% of the Brazilian respondents would be fully confident; 37.1% of them would be worried, but would accept the treatment; 11.3% would probably not accept the biosimilar and 11.3% would ask another physician. There was no significant statistical difference between Brazilian and non-Brazilian IBD patients (Table 2).

Pharmacist handing out the biosimilar

If the pharmacist handed out the biosimilar and changed the initial prescription without the consent of the prescribing physician, 82.3% of the Brazilian and 64.6% of the non-Brazilian respondents (p value 0.03) would try to obtain the reference drug (Table 2).

After starting biosimilar treatment

After starting a treatment with biosimilars, 50.0% of the Brazilian respondents would carefully follow the treatment, 22.6% would be worried and probably would stop treatment at the first doubt or adverse event, and 27.4% would be worried, but the fact that treatment was approved by the EMA would reassure them. There was no significant statistical difference between Brazilian and non-Brazilian IBD patients (Table 2).

Biosimilars and generic drugs

After receiving a definition of what generic drugs are, 17.7% of Brazilian IBD patients believed that biosimilars are like generic drugs, 12.9% of the respondents believed that biosimilars are close to generic drugs, 50.0% of the respondents believed that biosimilars are not at all like generics, and 19.4% did not know. Finally, 37.1% of the respondents reported that they take generic drugs without worries; 41.9% of the respondents accept generic drugs, but have some doubts, and 11.3% of the respondents reported that they refuse generic treatments whenever they can (Table 2).

Quality of information and communication on biosimilars

A question was added in the current survey about how the respondents would grade, on a scale from 0 (very poor) to 10 (excellent), the

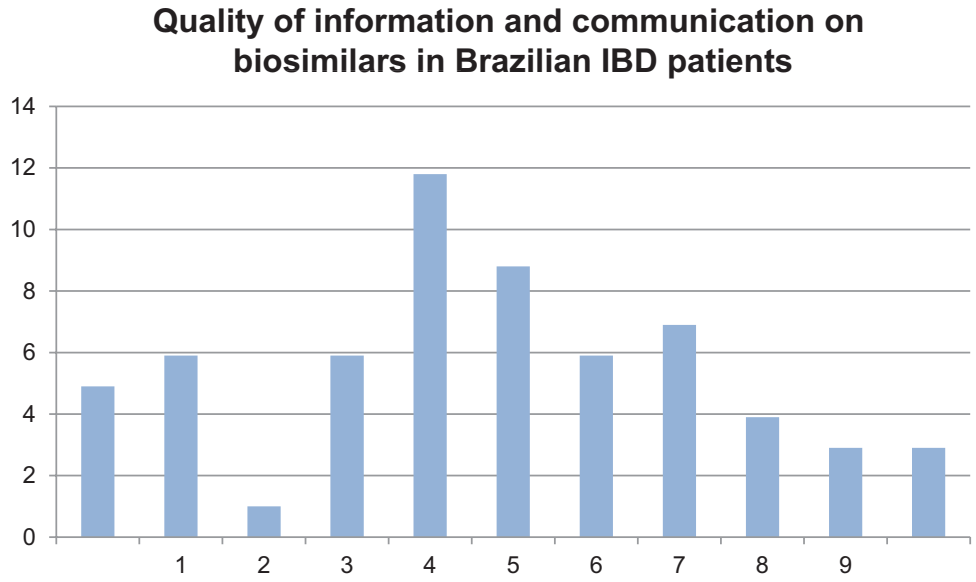

Figure 1. Quality of information and communication on biosimilars (%).
IBD, inflammatory bowel disease.

quality of information/communication that they received so far on biosimilars. Results are shown in Figure 1. In another new question, the respondents receiving biosimilars were asked whether they have been systematically informed by their doctors. Some of the respondents (18.2%) said they had, and 33.3% said they had not; for 42.4%, the question was not applicable (Figure 1).

Biosimilar efficacy and side effects in patients who have been switched

In two more questions, respondents were asked about their experiences on efficacy and side effects if they had been switched from Remicade to a biosimilar. Only 6.1% of the respondents reported to be experiencing the same efficacy, and 12.1% reported not. For 75.6% of the respondents, the question was not applicable. In addition, 4.5% of the respondents reported experiencing more side effects than before. For 78.8% of the respondents, the question was not applicable.

Discussion

Our study assessed Brazilian IBD patients' perceptions regarding biosimilars through a subanalysis of a previous survey[10] performed by EFCCA. Our findings highlight that concerns about use of biosimilars still remain among Brazilian IBD patients, which may reflect the lack of reassuring information about these drugs in the current scenario.

As in the non-Brazilian population, the majority (78.4%) of Brazilian patients had been exposed to anti-TNF drugs, and 67.6% of Brazilian respondents were being treated with that class of biologic at the time of the survey, while just 49.8% of non-Brazilian patients were currently using it. That significant statistical difference could be explained by the fact that anti-TNF drugs are the only biologic class available for IBD treatment in the Brazilian public health system.

Given that biosimilars for IBD were just recently introduced in Brazil (2015),[7] it was unexpected that 63.4% of Brazilians had been told about biosimilars as compared with 44.0% of the overall IBD population.[10] This information could reflect different educational strategies regarding biosimilars in each country. In addition, Brazilian patients reported higher rates of misconceptions regarding biosimilars, demonstrating that they probably have superficial knowledge on the topic. For instance, many concerns regarding biosimilars were shown, especially about their efficacy (62.5%), but also about non-similar molecular structure, safety and tolerability. Accordingly, only 14.3% of Brazilian IBD patients had been exposed to infliximab (IFX) biosimilar. We

speculate that the low uptake of biosimilars in the Brazilian population may have contributed to their uncertainties.

These findings raise awareness regarding the possible nocebo effect, defined as a negative effect of a medical treatment that is related to patients' expectations and unrelated to the drugs' physiological action, that may be induced as a result of a negative attitude toward an intervention.[11] Experiences shared by patients as well as media information may influence perceptions of biosimilars, contributing to nocebo effects.[12] Our data reinforce the need for proper patient education concerning the biosimilars in order to decrease hesitation, clarify doubts and to provide greater adherence to biosimilars. Interestingly, although the worries remain, respondents were significantly more likely to believe that biosimilars would have an impact on the management of IBD (69.2%).

Although the results reinforce that patients have a basic knowledge on biosimilars, they do want to be involved when the physician chooses their treatment. They emphasized the desire to be informed when starting a biosimilar; however, some patients still disclosed they would probably not accept the biosimilar (13.3%) or they would ask for another expert opinion (13.3%). Informing patients during the medical appointment or *via* patient's organizations could be a way to provide a better understanding and to build confidence on biosimilars. It is also important to inform patients on immunogenicity and other safety issues.

In a hypothetical situation in which treatment with biosimilars was started, just half of the patients committed to follow the treatment, and 22.6% of the Brazilians said that they would stop the treatment at the first doubt or adverse event. These results emphasize data from a recently published meta-analysis that included 3594 IBD patients who switched from originator to biosimilars in real-world cohorts that had discontinuation rates of 8%, 14%, and 21% at 6, 12, and 24 months, respectively. The most common causes of discontinuation were loss of response (5%) and adverse events (7%).[13]

This survey had several limitations. It was self-selective, only available online in a European website in eight languages (including Portuguese), which may have contributed to the low access of Brazilians to the questionnaire. Moreover, the results of this study might not be representative for the population who lives in Brazil, due to the small sample and the lack of information regarding the region where the patients live.

In conclusion, despite rigorous approval processes by regulatory entities, Brazilian IBD patients' knowledge regarding biosimilars is more limited than that observed for non-Brazilian IBD patients, and some concerns about their use persist. Increasing knowledge of patients and professionals on safety and efficacy of biosimilars could minimize negative expectations about these drugs as treatment options.[8,14] Moreover, we believe that the widespread use and experience with biosimilars from now on in Brazil will pave the way for increased confidence with these drugs. Our study reinforces European Crohn's and Colitis Organization recommendations[15] that a switch should be based on collaborative decision making, benefiting individual patients, rather than systematic non-medical decisions that can compromise safety and treatment adherence.

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Conflict of interest statement

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Ethical statements

The participants of the survey were members of EFCCA member associations or persons following the communications of these associations. Informed consent was waived since the survey recruitment was self-selective. In addition, data were de-identified and individual participant data were not published, which maintained confidentiality in all steps of study analysis. This study was conducted in compliance with regulations stated in the 1975 Declaration of Helsinki.

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References

1. Lamb CA, Kennedy NA, Raine T, *et al.* British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut* 2019; 68: s1–s106.
2. Park KT, Ehrlich OG, Allen JI, *et al.* The cost of inflammatory bowel disease: an initiative from the Crohn's & Colitis Foundation. *Inflamm Bowel Dis* 2020; 26: 1–10.
3. Pillai N, Dusheiko M, Maillard MH, *et al.* The evolution of health care utilisation and costs for inflammatory bowel disease over ten years. *J Crohns Colitis* 2019; 13: 744–754.
4. European Medicines Agency, European Commission. *Biosimilars in the EU: information guide for healthcare professionals*. London: European Medicines Agency; 2017. https://www.ema.europa.eu/en/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf
5. Danese S, Bonovas S and Peyrin-Biroulet L. Biosimilars in IBD: from theory to practice. *Nat Rev Gastroenterol Hepatol* 2017; 14: 22–31.
6. Agência Nacional de Vigilância Sanitária (Brasil). Resolução no. 784, de 28 de março de 2019. Medicamentos e Produtos Biológicos. Diário Oficial da União 1 April 2019; Seção 1.
7. Teixeira FV, Kotze PG and Damião AOMC. Anvisa approves the first biosimilar monoclonal antibody based on comparability in Brazil. *Arquivos de Gastroenterologia* 2016; 53: 60–61.
8. Greene L, Singh RM, Carden MJ, *et al.* Strategies for overcoming barriers to adopting biosimilars and achieving goals of the biologics price competition and innovation act: a survey of managed care and specialty pharmacy professionals. *J Manag Care Spec Pharm* 2019; 25: 904–912.
9. Kim H, Alten R, Avedano L, *et al.* The future of biosimilars: maximizing benefits across immune-mediated inflammatory diseases. *Drugs* 2020; 80: 99–113. Erratum in: *Drugs* 2020; 80: 1039–1040.
10. Peyrin-Biroulet L, Lönnfors S, Avedano L, *et al.* Changes in inflammatory bowel disease patients' perspectives on biosimilars: a follow-up survey. *United European Gastroenterol J* 2019; 7: 1345–1352.
11. Pouillon L, Danese S, Hart A, *et al.* Consensus report: clinical recommendations for the prevention and management of the nocebo effect in biosimilar-treated IBD patients. *Aliment Pharmacol Ther* 2019; 49: 1181–1187.
12. Pouillon L, Socha M, Demore B, *et al.* The nocebo effect: a clinical challenge in the era of biosimilars. *Expert Rev Clin Immunol* 2018; 14: 739–749.
13. Queiroz NSF, Saad-Hossne R, Fróes RSB, *et al.* Discontinuation rates following a switch from a reference to a biosimilar biologic in patients with inflammatory bowel disease: a systematic review and meta-analysis. *Arq Gastroenterol* 2020; 57: 232–243.
14. Solitano V, D'Amico F, Fiorino G, *et al.* Biosimilar switching in inflammatory bowel disease: from evidence to clinical practice. *Expert Rev Clin Immunol* 2020; 16: 1019–1028.
15. Danese S, Fiorino G, Raine T, *et al.* ECCO position statement on the use of biosimilars for inflammatory bowel disease-an update. *J Crohns Colitis* 2017; 11: 26–34.