Is Similar the Same? How We Incorporated Feedback from 250 Patients into a CME Activity on Biosimilars

Stephen Bender[1] and Suzanne Schrandt[2] • [1]FACTORx, Cherry Hill, NJ, [2]ExPPect, Arlington, VA

GOALS

The goals of this project are two-fold: The primary goal is to provide clinicians who treat rheumatoid arthritis (RA) and inflammatory bowel disease (IBD) patients with a better understanding of the manufacturing process for biosimilars and secondarily, present the major patient questions and concerns when it comes to switching from an originator therapy to a biosimilar so that both the clinicians and patients are better prepared for those discussions. Informed through feedback from a patient survey, the multi-stakeholder discussion generated ideas for patient-friendly terminology and educational resources to which patients can be referred.

BACKGROUND

Rheumatoid arthritis (RA) and inflammatory bowel disease (IBD); are chronic, systemic, autoimmune disorders. Appropriate therapy for these diseases includes treatment with disease-modifying antirheumatic drugs (DMARDs). All of the FDA-approved biologic therapies target specific pathways involved in the pathophysiology of RA and IBD, and interfere with the inflammatory activity associated with these diseases.[7-10] A number of biosimilar DMARDs are currently approved by Food and Drug Administration (FDA), or are being tested for managing RA and IBD.[1-6] These emerging drug options may be less costly, as new technologies have allowed for the reproduction of some of the original targeted agents.

The availability of these potentially lower cost biosimilars may help to increase accessibility to effective biopharmaceutical therapy while maintaining efficacy and safety similar to the originator drugs.[15,16] However, biosimilars are not identical to the originator (reference) drugs, and clinicians may be concerned not only for safety and efficacy issues, but also for the immunogenicity of these drugs.[15,17,18] Thus, there are several barriers to greater use of these biosimilar drugs by practitioners.[1]

Clinicians and patients must also understand the differences between switching, substitution, and interchangeability.

This learning activity, co-designed by RA and IBD patients and clinicians, was developed to address these knowledge gaps and concerns of patients and clinicians, and provide practical tools for better informing and navigating treatment discussions. The faculty agreed that rheumatologists, gastroenterologists, PCPs, pharmacists, and patients all had a role to play in understanding the benefit/risk assessment of all therapeutic options and reaching a consensus for treatment. The value of patient participation in evaluating the benefit/risk equation has been noted by the FDA in a recent statement: "Patient experiences and insight can help us understand the benefits most important to patients and what risks patients may or may not be willing to tolerate."[26] Patient participation in medical education has also been found to be beneficial in other clinical areas, and notably ACR's "Patient Perspective" poster program elevates the lived experience of patients as valuable teaching tools.[27,28]

PROJECT DESIGN

The inclusion of patients in the content development phase helped provide both the clinical faculty and the patients with insight that would not otherwise have been uncovered. To be most impactful, patient engagement in medical education must be carefully planned and integrated into the programming. Too often patient engagement is misconceived as taking a moment in the agenda for a patient to share a "sad story", but that model fails to capitalize on the immense lived experience of patients to reinforce learning objectives and make content tangible. In this project, the lived experience of patients was a foundational building block, with the survey results informing the discussion points and driving the clinical content.

The content was designed as a one-hour, enduring panel discussion distributed online that carried both ACCME and ACPE accreditation. The panel discussion was comprised of a rheumatologist, a gastroenterologist, an IBD patient and an RA patient. The learning objectives and discussion points were informed by key data points from the survey, fielded amongst 246 IBD (N=101) and RA (N=145) patients.

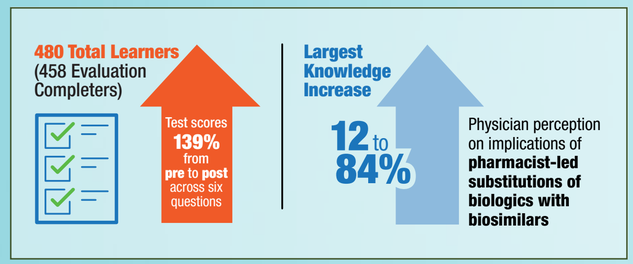
OUTCOMES/CONCLUSIONS

This CME initiative was unique in the fact that we conducted a survey amongst 250+ RA and IBD patients to assess baseline knowledge around biosimilars, interactions with their providers, concerns around switching to a biosimilar, most trusted sources of medical information, and the factors that would make them more or less likely to feel comfortable with a switch. The survey results were presented to our patient and clinical faculty to help serve as the foundation for the panel discussion but also to prepare both the clinicians and patients for some of the challenging discussions they're likely to encounter.

Clinician Outcomes: Satisfaction levels: mean of 4.32 out of 5 ratings across 5 aspects of activity quality and achievement of learning objectives. Of learners, 55% felt more prepared to answer patient questions about biosimilars, and 50% felt better able to explain to their colleagues when and how biosimilars can be safely used. 27% would be more likely (after accessing this content) to consider switching from a biologic to a biosimilar as appropriate in patients with RA or IBD. Top barriers to practice change were insurance, reimbursement or legal issues (41%), lack of knowledge regarding evidence-based strategies (36%) and patient comfort with switching and likelihood to be compliant with the switch (35%).

Overall there were 480 total learners (started content), with 458 evaluation completers. Test scores increased by 139% (**Figure 1**) across 6 questions from pre (39% correct, SD 24.7) to post (93% correct, SD 0.9) with a large effect size (Cohen's d = 1.93). Most notable knowledge increase: (**Figure 1**) 7-fold increase in correct answers from pre (12%) to post (84%) regarding the fact that, according to a systematic review of physician perception on biosimilar uptake in 9 different studies, the "implications of pharmacist-led substitution of biologics with biosimilars" was cited as a concern by the majority of the physicians.

Figure 1



FACTORx conducted a national-scope medical claims analysis called, *The Potential Patient Impact Factor Analysis*, to objectively determine the minimum number of RA and IBD patients managed/treated annually by the learners of this initiative. Of the 466 learners, we identified 91 who were actively managing/treating RA/IBD patients in the last year. These 91 learners alone managed a minimum of 53,318 patient treatments annually for their RA and IBD patients.

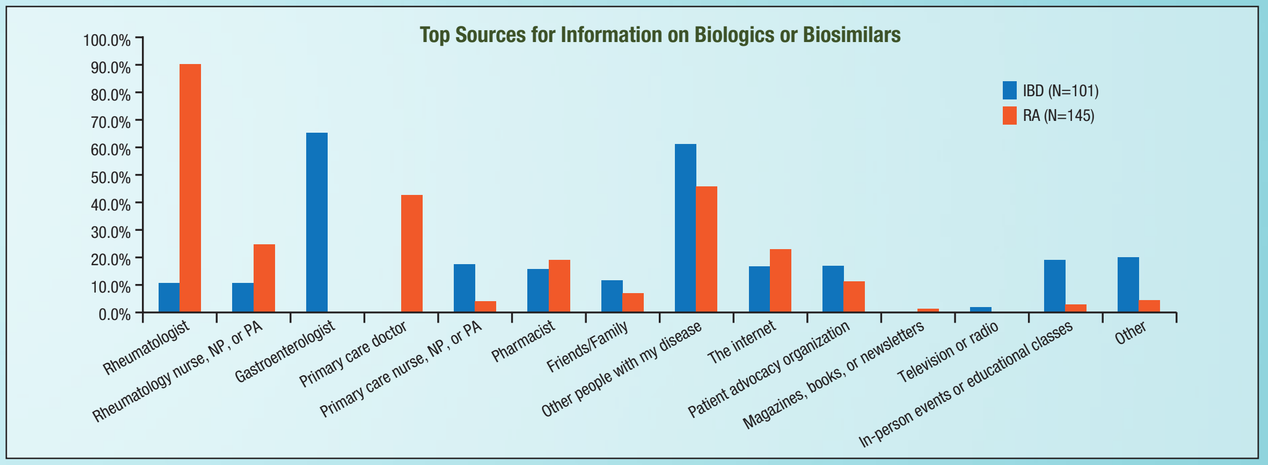
Patient Survey Highlights: Although the data from our patient survey did not reveal any specific statistically significant trends, there is quite a bit of anecdotal and experiential evidence that patients who have already been on biologics may have more concerns about or be less willing to switch to a biosimilar. This was due to their prior experience having worked hard to achieve optimal disease management through therapeutic trial and error, and not wanting to "upset the applecart" by switching to a biosimilar. Another fear was being forced to switch without having any input or control in the matter. In fact, many of the free text answers below speak to these phenomena:

- "The biggest concern with biosimilars for me is insurance forcing the switch."
- "Just because it is similar does not mean that it will give you remission like the biologic. Then you most likely can't go back to the biologic since you were off of the biologic and antibodies to it were built up."
- "Remission has been hard to achieve even with biologics so I'm not certain how a biosimilar would make a difference."
- "Insurance making the switch while the biologic medication has you in remission."
- "Terrified to take new medication"

Consistent with other patient surveys that we've conducted, the second most-trusted source (**Figure 2**) for information behind the patient's treating specialist is 'other patients with my disease.' Providing informational materials directly to patients and referring patients to reliable patient advocacy organizations can be a valuable support mechanism for supporting education and participation in treatment decision-making.

Observations/Conclusions: Including the patient's voice in the creation and delivery of CME content is helpful but collecting input from multiple patients can bring more insight into an initiative. The optimal approach, undertaken here, is a combination of both; involving patient faculty to help design the survey and participate in data analysis, and gathering quantitative data from a wide swath of diverse patients to get a broader perspective of experience.

Figure 2



REFERENCES

1. Kos IA, Azevedo VF, Neto DE, Kowalski SC. The biosimilars journey: current status and ongoing challenges. *Drugs in context.* 2018;7:212543.
2. Argollo M, Fiorino G, Gilardi D, et al. Biosimilars of Adalimumab in Inflammatory Bowel Disease: Are we Ready for that? *Curr Pharm Des.* 2019;25(1):7-12.
3. Cohen S, Genovese MC, Choy E, et al. Efficacy and safety of the biosimilar ABP 501 compared with adalimumab in patients with moderate to severe rheumatoid arthritis: a randomised, double-blind, phase III equivalence study. *Ann Rheum Dis.* 2017;76(10):1679-1687.
4. Milassin A, Fabian A, Molnar T. Switching from infliximab to biosimilar in inflammatory bowel disease: overview of the literature and perspective. *Therap Adv Gastroenterol.* 2019;12:17562848198427 48.
5. Weinblatt ME, Baranauskaite A, Niebrzydowski J, et al. Phase III Randomized Study of SB5, an Adalimumab Biosimilar, Versus Reference Adalimumab in Patients With Moderate-to-Severe Rheumatoid Arthritis. *Arthritis & rheumatology (Hoboken, NJ).* 2018;70(1):40-48.
6. FDA-Approved Biosimilar Products: https://www.fda.gov/drugs/biosimilars/biosimilar-product-information Accessed February 3, 2020.
7. Wang D, Li Y, Liu Y, Shi G. The use of biologic therapies in the treatment of rheumatoid arthritis. *Curr Pharm Biotechnol.* 2014;15(6):542-548.
8. Edwards JC, Szczepanski L, Szechinski J, et al. Efficacy of B-cell-targeted therapy with rituximab in patients with rheumatoid arthritis. *N Engl J Med.* 2004;350(25):2572-2581.
9. Oldfield V, Dhillon S, Plosker GL. Tocilizumab: a review of its use in the management of rheumatoid arthritis. *Drugs.* 2009;69(5):609-632.
10. Wheat CL, Ko CW, Clark-Snustad K, Grembowski D, Thornton TA, Devine B. Inflammatory Bowel Disease (IBD) pharmacotherapy and the risk of serious infection: a systematic review and network meta-analysis. *BMC Gastroenterol.* 2017;17(1):52.
11. Smolen JS, Landewe R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. *Ann Rheum Dis.* 2014;73(3):492-509.
12. Lapadula G, Ferraccioli GF. Biosimilars in rheumatology: pharmacological and pharmacoeconomic issues. *Clin Exp Rheumatol.* 2012;30(4 Suppl 73):S102-106.
13. Cohen S, Kay J. Biosimilars: implications for rheumatoid arthritis therapy. *Curr Opin Rheumatol.* 2017;29(3):260-268.
14. Avila-Ribeiro P, Fiorino G, Danese S. The Experience with Biosimilars of Infliximab in Inflammatory Bowel Disease. *Curr Pharm Des.* 2017;23(44):6759-6769.
15. Dorner T, Strand V, Cornes P, et al. The changing landscape of biosimilars in rheumatology. *Ann Rheum Dis.* 2016;75(6):974-982.
16. Kay J, Smolen JS. Biosimilars to treat inflammatory arthritis: the challenge of proving identity. *Ann Rheum Dis.* 2013;72(10):1589-1593.
17. Scheinberg MA, Azevedo VF. Biosimilars in rheumatology: perspective and concerns. *Rheumatology (Oxford).* 2014;53(3):389-390.
18. Dorner T, Kay J. Biosimilars in rheumatology: current perspectives and lessons learnt. *Nat Rev Rheumatol.* 2015;11(12):713-724.
19. Schiestl M, Stangler T, Torella C, Cepeljnik T, Toll H, Grau R. Acceptable changes in quality attributes of glycosylated biopharmaceuticals. *Nat Biotechnol.* 2011;29(4):310-312.
20. Visser J, Feuerstein I, Stangler T, Schmiederer T, Fritsch C, Schiestl M. Physicochemical and functional comparability between the proposed biosimilar rituximab GP2013 and originator rituximab. *Biodrugs.* 2013;27(5):495-507.
21. FDARegulatory.net. Biologics Price Competition and Innovation Act. 2010. http://fdaregulatory.net/index.php/fda-regulatory-articles/buiologics. Accessed April 5, 2017.
22. FDA. Biosimilar Product Review and Approval. 2019; https://www.fda.gov/media/108621/download. Accessed September 30, 2019.
23. Smolen JS, Goncalves J, Quinn M, Benedetti F, Lee JY. Era of biosimilars in rheumatology: reshaping the healthcare environment. *RMD open.* 2019;5(1):e000900.
24. Glintborg B, Ibsen R, Bilbo REQ, Lund Hetland M, Kjellberg J. Does a mandatory non-medical switch from originator to biosimilar etanercept lead to increase in healthcare use and costs? A Danish register-based study of patients with inflammatory arthritis. *RMD open.* 2019;5(2):e001016.
25. Mulcahy A, Predmore Z, Mattke S. The cost savings potential of biosimilar drugs in the United States. 2014. http://www.rand.org/pubs/perspectives/PE127.html. Accessed April 4, 2017.
26. FDA. Statement on FDA efforts to encourage patient engagement in medical device clinical investigations. 2019; https://www.fda.gov/news-events/press-announcements/statement-fda-efforts-encourage-patient-engagement-medical-device-clinical-investigations.
27. Klein S, Tracy D, Kitchener HC, Walker LG. The effects of the participation of patients with cancer in teaching communication skills to medical undergraduates: a randomised study with follow-up after 2 years. *Eur J Cancer.* 2000;36(2):273-281.
28. American College of Rheumatology, Patient Perspectives, https://www.rheumatology.org/Annual-Meeting/Program, accessed, September 28, 2022.