**Supplementary Table 1. Integral survey with responses**

|  |  |  |
| --- | --- | --- |
| SURVEY ON THE USE OF BIOSIMILARS |  |  |
| Q1. Age in years: |  |  |
| **Answered** | **234** |  |
| **Skipped** | **0** |  |
|  |  |  |
| Q2. Sex |  |  |
| Answer Choices | Responses | |
| Male | 56.41% | 132 |
| Female | 43.59% | 102 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q3. What country do you work in? |  |  |
| **Answered** | **234** |  |
| **Skipped** | **0** |  |
|  |  |  |
| Q4. What is your specialization? |  |  |
| Answer Choices | Responses | |
| Gastroenterologist | 86.32% | 202 |
| Internal doctor | 1.28% | 3 |
| Surgeon | 2.56% | 6 |
| General practitioner | 1.28% | 3 |
| Other (please specify) | 8.55% | 20 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q5. How many years of experience do you have in the field of IBD? | | |
| Answer Choices | Responses | |
| Less than 1 year | 0.43% | 1 |
| Less than 5 years | 6.84% | 16 |
| Less than 10 years | 18.38% | 43 |
| More than 10 years | 74.36% | 174 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q6. How many IBD patients do you see per year? | |  |  |
| Answer Choices | Responses | |
| Less than 100 | 24.36% | 57 |
| Less than 500 | 38.46% | 90 |
| Less than 1000 | 23.93% | 56 |
| More than 1000 | 13.25% | 31 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q7. In your opinion, which of the following statements is correct? | | |
| Answer Choices | Responses | |
| Biosimilars are as effective and safe as the originator drugs | 83.33% | 195 |
| Biosimilars are as effective but less safe than the originator drugs | 3.42% | 8 |
| Biosimilars are as safe but less effective than the originator drugs | 6.41% | 15 |
| Biosimilars are less effective and less safe than the originator drugs | 3.85% | 9 |
| Do not know | 2.99% | 7 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q8. How confident are you about the use of biosimilars using a scale from 0 (lowest value) to 10 (highest value)? | | |
|  | 1 (lowest value= | |
| star | 1.28% | 3 |
|  |  |  |
|  |  |  |
|  |  |  |
| Q9. How confident are your patients about the use of biosimilars using a scale from 0 (lowest value) to 10 (highest value)? | | |
|  | 1 (lowest value= | |
| star | 0.85% | 2 |
|  |  |  |
|  |  |  |
|  |  |  |
| Q10. Do you think the data on biosimilars extrapolated from other immune mediated inflammatory diseases are also valid in IBD? | | |
| Answer Choices | Responses | |
| Yes | 75.21% | 176 |
| No | 24.79% | 58 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q11. Do you think patients should be informed about what a biosimilar is before starting therapy? | | |
| Answer Choices | Responses | |
| Yes | 83.33% | 195 |
| No | 16.67% | 39 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q12. Who should provide information to patients about biosimilars? | | |
| Answer Choices | Responses | |
| Physician (gastroenterologist, internal doctor etc) | 86.75% | 203 |
| Resident | 0.85% | 2 |
| Nurse | 3.85% | 9 |
| Pharmacist | 2.56% | 6 |
| Government authorities | 2.56% | 6 |
| Payers/Insurance | 1.28% | 3 |
| Other (please specify) | 2.14% | 5 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q13. Before prescribing a biological drug, do you explain to patients what a biosimilar drug is and what the originator drug is? | | |
| Answer Choices | Responses | |
| Yes | 70.51% | 165 |
| No | 29.49% | 69 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q14. Do you provide patients with data comparing biosimilars and originator drugs? | | |
| Answer Choices | Responses | |
| Yes | 32.91% | 77 |
| No | 67.09% | 157 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q15. Do you provide written materials to patients informing them on the use of biosimilars? | | |
| Answer Choices | Responses | |
| Yes | 26.07% | 61 |
| No | 73.93% | 173 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q16. Have you ever prescribed biosimilars of infliximab? | | |  |
| Answer Choices | Responses | |
| Yes | 87.61% | 205 |
| No | 12.39% | 29 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q17. Have you ever prescribed biosimilars of adalimumab? | | |  |
| Answer Choices | Responses | |
| Yes | 83.76% | 196 |
| No | 16.24% | 38 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q18. Do you think biosimilars should only be prescribed to naïve patients? | | |
| Answer Choices | Responses | |
| Yes | 19.23% | 45 |
| No | 72.22% | 169 |
| Do not know | 8.55% | 20 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q19. Have you ever switched a patient from the originator drug to the biosimilar? | | |
| Answer Choices | Responses | |
| Yes | 81.62% | 191 |
| No | 18.38% | 43 |
|  | **Answered** | **234** |
|  | **Skipped** | **0** |
|  |  |  |
| Q20. If you answered yes to question 19, why did you switch from the originator drug to the biosimilar? | | |
| Answer Choices | Responses | |
| Due to the lower cost of the biosimilar | 54.74% | 104 |
| Due to allergic reaction to the originator drug | 1.05% | 2 |
| Due to a loss of response to the originator drug | 2.11% | 4 |
| Due to unavailability of the originator drug | 15.79% | 30 |
| Efficacy comparable to the originator drug | 3.16% | 6 |
| Safety comparable to the originator drug | 0.00% | 0 |
| Efficacy and safety comparable to the originator drug | 10.00% | 19 |
| Other (please specify) | 13.16% | 25 |
|  | **Answered** | **190** |
|  | **Skipped** | **44** |
|  |  |  |
| Q21. When do you switch from the originator to the biosimilar? | | |  |
| Answer Choices | Responses | |
| When the patient achieves clinical remission | 5.50% | 12 |
| When the patient achieves biochemical remission (normal CRP and/or fecal calprotectin) | 1.83% | 4 |
| When the patient achieves both clinical remission and biochemical remission | 15.14% | 33 |
| When the patient achieves endoscopic remission | 4.59% | 10 |
| Regardless of disease activity | 16.97% | 37 |
| It is a non-medical decision | 55.96% | 122 |
|  | **Answered** | **218** |
|  | **Skipped** | **16** |
|  |  |  |
| Q22. Do you monitor drug trough levels and autoantibodies in patients switched to biosimilars? | | |
| Answer Choices | Responses | |
| Yes | 43.12% | 94 |
| No | 56.88% | 124 |
|  | **Answered** | **218** |
|  | **Skipped** | **16** |
|  |  |  |
| Q23. Do you have patients who have refused to start therapy with a biosimilar or switch to a biosimilar? | | |
| Answer Choices | Responses | |
| Yes | 46.79% | 102 |
| No | 53.21% | 116 |
|  | **Answered** | **218** |
|  | **Skipped** | **16** |
|  |  |  |
| Q24. If you have patients who refused to be treated with a biosimilar, what is the proportion of these patients? | | |
| Answer Choices | Responses | |
| <1% | 63.30% | 138 |
| <5% | 19.27% | 42 |
| <10% | 7.34% | 16 |
| <25% | 6.88% | 15 |
| <50% | 1.83% | 4 |
| ≥50% | 1.38% | 3 |
|  | **Answered** | **218** |
|  | **Skipped** | **16** |
|  |  |  |
| Q25. What is the main reason for patients' refusal of the biosimilar? | | |
| Answer Choices | Responses | |
| Fear that the drug is not effective | 36.24% | 79 |
| Fear that the drug is not safe | 7.80% | 17 |
| Fear that the switch will be made due to a cost issue, neglecting the patient's health | 14.22% | 31 |
| Fear that the switch may be associated with disease relapse | 23.85% | 52 |
| Other (please specify) | 17.89% | 39 |
|  | **Answered** | **218** |
|  | **Skipped** | **16** |
|  |  |  |
| Q26. Despite the availability of biosimilars, do you prescribe originator drugs? | | |
| Answer Choices | Responses | |
| Yes | 61.01% | 133 |
| No | 38.99% | 85 |
|  | **Answered** | **218** |
|  | **Skipped** | **16** |
|  |  |  |
| Q27. If you prescribe originator drugs despite the availability of the biosimilars, why do you prefer the originator drug? | | |
| Answer Choices | Responses | |
| Originator drugs are more effective than biosimilars | 7.34% | 16 |
| Originator drugs are safer than biosimilars | 2.75% | 6 |
| Originator drugs are more effective and safer than biosimilars | 3.21% | 7 |
| I have no biosimilars available in my hospital | 11.93% | 26 |
| There is little data on biosimilars, I prefer the originator drugs because there is more scientific evidence | 17.43% | 38 |
| Other (please specify) | 57.34% | 125 |
|  | **Answered** | **218** |
|  | **Skipped** | **16** |
|  |  |  |
| Q28. In a patient candidate for biologic therapy, have you ever started IBD therapy using biosimilars? | | |
| Answer Choices | Responses | |
| Yes | 89.91% | 196 |
| No | 10.09% | 22 |
|  | **Answered** | **218** |
|  | **Skipped** | **16** |
|  |  |  |
| Q29. In a patient who started a biosimilar as first drug, have you ever switched to the originator drug? | | |
| Answer Choices | Responses | |
| Yes | 26.15% | 57 |
| No | 73.85% | 161 |
|  | **Answered** | **218** |
|  | **Skipped** | **16** |
|  |  |  |
| Q30. If you answered yes to question 29, why were the patients switched from the biosimilar to the originator drug (multiple answers are possible)? | | |
| Answer Choices | Responses | |
| Due to allergic reaction to the biosimilar | 14.81% | 8 |
| Due to a loss of response to the biosimilar | 27.78% | 15 |
| Due to unavailability of the biosimilar | 37.04% | 20 |
| Other (specify) | 3.70% | 2 |
| Other (please specify) | 16.67% | 9 |
|  | **Answered** | **54** |
|  | **Skipped** | **180** |
|  |  |  |
| Q31. If you answered yes to question 29, did patients switched from the biosimilar to the originator drug achieve/maintain disease remission? | | |
| Answer Choices | Responses | |
| Yes | 83.02% | 44 |
| No | 16.98% | 9 |
|  | **Answered** | **53** |
|  | **Skipped** | **181** |
|  |  |  |
| Q32. Have you ever switched from one biosimilar to another biosimilar of the same drug (multiple switch)? | | |
| Answer Choices | Responses | |
| Yes | 50.54% | 93 |
| No | 49.46% | 91 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q33. If you have multiple switched patients, why were the patients switched from one biosimilar to another (multiple answers are possible)? | | |
| Answer Choices | Responses | |
| Due to allergic reaction to the first biosimilar | 8.15% | 15 |
| Due to a loss of response to the first biosimilar | 9.24% | 17 |
| Due to unavailability of the first biosimilar | 44.02% | 81 |
| Other (please specify) | 44.57% | 82 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q34. Did multiple switched patients achieve/maintain disease remission? | | |
| Answer Choices | Responses | |
| Yes | 70.11% | 129 |
| No | 29.89% | 55 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q35. In a patient treated with the originator drug and then switched to the biosimilar, have you ever prescribed the reverse switch to the originator drug? | | |
| Answer Choices | Responses | |
| Yes | 39.13% | 72 |
| No | 60.87% | 112 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q36. If you have patients undergoing reverse switch, what was the reason for reverse switch (multiple answers are possible)? | | |
| Answer Choices | Responses | |
| Due to allergic reaction to the biosimilar | 13.04% | 24 |
| Due to a loss of response to the biosimilar | 16.30% | 30 |
| Due to unavailability of the biosimilar | 29.89% | 55 |
| Other (please specify) | 51.09% | 94 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q37. Did reverse switched patients achieve/maintain disease remission? | | |
| Answer Choices | Responses | |
| Yes | 69.57% | 128 |
| No | 30.43% | 56 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q38. Do you know what the nocebo effect is? | |  |  |
| Answer Choices | Responses | |
| Yes | 86.41% | 159 |
| No | 13.59% | 25 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q39. Have your patients ever experienced the nocebo effect? | | |  |
| Answer Choices | Responses | |
| Yes | 38.59% | 71 |
| No | 29.35% | 54 |
| Do not know | 32.07% | 59 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q40. If your patients experienced the nocebo effect, what is the rate of nocebo effect among your patients? | | |
| Answer Choices | Responses | |
| None | 50.54% | 93 |
| <5% | 30.98% | 57 |
| <10% | 12.50% | 23 |
| <25% | 4.89% | 9 |
| <50% | 0.54% | 1 |
| ≥50% | 0.54% | 1 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q41. Do you have patients who underwent a non-medical switch? | | |
| Answer Choices | Responses | |
| Yes | 57.07% | 105 |
| No | 42.93% | 79 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q42. Did non-medical switched patients achieve/maintain disease remission? | | |
| Answer Choices | Responses | |
| Yes | 67.39% | 124 |
| No | 32.61% | 60 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q43. Does the presence of biosimilars have an impact on your therapeutic choices? | | |
| Answer Choices | Responses | |
| Yes | 73.91% | 136 |
| No | 26.09% | 48 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q44. In the near future, will you be prescribing biosimilars of vedolizumab, ustekinumab, and tofacitinib? | | |
| Answer Choices | Responses | |
| Yes | 74.46% | 137 |
| No | 2.17% | 4 |
| Do not know | 23.37% | 43 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q45. Do you think the availability of the biosimilars of vedolizumab, ustekinumab, and tofacitinib will change the treatment algorithm of IBD patients? | | |
| Answer Choices | Responses | |
| Yes | 52.17% | 96 |
| No | 30.43% | 56 |
| Do not know | 17.39% | 32 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |
|  |  |  |
| Q46. How would you implement the use of biosimilars in clinical practice (multiple answers are possible)? | | |
| Answer Choices | Responses | |
| There is a need to conduct randomized clinical trials to compare the efficacy and safety of biosimilars and originator drugs in patients with IBD | 38.59% | 71 |
| Long term data are needed | 50.54% | 93 |
| Non-medical switch | 24.46% | 45 |
| Patient engagement in the therapeutic decision | 32.07% | 59 |
| More information should be provided to health care providers | 26.63% | 49 |
| Government authorities should provide more information to patients about the efficacy and safety of biosimilars | 32.61% | 60 |
| Patient associations should provide more information on biosimilars | 28.80% | 53 |
| Other | 4.35% | 8 |
|  | **Answered** | **184** |
|  | **Skipped** | **50** |

**Supplementary Table 2. CROSS checklist**

|  |  |  |  |
| --- | --- | --- | --- |
| **Section/topic** | **Item** | **Item description** | **Reported on page #** |
| **Title and abstract** | | |  |
| Title and abstract | 1a | State the word “survey” along with a commonly used term in title or abstract to introduce the study’s design. | 3,4 |
| 1b | Provide an informative summary in the abstract, covering background, objectives, methods, findings/results, interpretation/discussion, and conclusions. | 3 |
| **Introduction** | | |  |
| Background | 2 | Provide a background about the rationale of study, what has been previously done, and why this survey is needed. | 4 |
| Purpose/aim | 3 | Identify specific purposes, aims, goals, or objectives of the study. | 4 |
| **Methods** | | |  |
| Study design | 4 | Specify the study design in the methods section with a commonly used term (e.g., cross-sectional or longitudinal). | 5,6 |
|  | 5a | Describe the questionnaire (e.g., number of sections, number of questions, number and names of instruments used). | 5,6 |
| Data collection methods | 5b | Describe all questionnaire instruments that were used in the survey to measure particular concepts. Report target population, reported validity and reliability information, scoring/classification procedure, and reference links (if any). | 5,6 |
| 5c | Provide information on pretesting of the questionnaire, if performed (in the article or in an online supplement). Report the method of pretesting, number of times questionnaire was pre-tested, number and demographics of participants used for pretesting, and the level of similarity of demographics between pre-testing participants and sample population. | 5,6 |
| 5d | Questionnaire if possible, should be fully provided (in the article, or as appendices or as an online supplement). | Yes, in Data Suppl. |
| Sample characteristics | 6a | Describe the study population (i.e., background, locations, eligibility criteria for participant inclusion in survey, exclusion criteria). | 5 |
| 6b | Describe the sampling techniques used (e.g., single stage or multistage sampling, simple random sampling, stratified sampling, cluster sampling, convenience sampling). Specify the locations of sample participants whenever clustered sampling was applied. |  |
| 6c | Provide information on sample size, along with details of sample size calculation. | NA |
| 6d | Describe how representative the sample is of the study population (or target population if possible), particularly for population-based surveys. | NA |
| Survey  administration | 7a | Provide information on modes of questionnaire administration, including the type and number of contacts, the location where the survey was conducted (e.g., outpatient room or by use of online tools, such as SurveyMonkey). | 6 |
| 7b | Provide information of survey’s time frame, such as periods of recruitment, exposure, and follow-up days. | 6 |
| 7c | Provide information on the entry process:  –>For non-web-based surveys, provide approaches to minimize human error in data entry.  –>For web-based surveys, provide approaches to prevent “multiple participation” of participants. | 6 |
| Study preparation | 8 | Describe any preparation process before conducting the survey (e.g., interviewers’ training process, advertising the survey). | NA |
| Ethical considerations | 9a | Provide information on ethical approval for the survey if obtained, including informed consent, institutional review board [IRB] approval, Helsinki declaration, and good clinical practice [GCP] declaration (as appropriate). | 5 |
| 9b | Provide information about survey anonymity and confidentiality and describe what mechanisms were used to protect unauthorized access. | 5 |
| Statistical  analysis | 10a | Describe statistical methods and analytical approach. Report the statistical software that was used for data analysis. | 6 |
| 10b | Report any modification of variables used in the analysis, along with reference (if available). | NA |
| 10c | Report details about how missing data was handled. Include rate of missing items, missing data mechanism (i.e., missing completely at random [MCAR], missing at random [MAR] or missing not at random [MNAR]) and methods used to deal with missing data (e.g., multiple imputation). | 5 |
| 10d | State how non-response error was addressed. | NA |
| 10e | For longitudinal surveys, state how loss to follow-up was addressed. | NA |
| 10f | Indicate whether any methods such as weighting of items or propensity scores have been used to adjust for non-representativeness of the sample. | NA |
| 10g | Describe any sensitivity analysis conducted. | NA |
| **Results** | | |  |
| Respondent characteristics | 11a | Report numbers of individuals at each stage of the study. Consider using a flow diagram, if possible. | 8 |
| 11b | Provide reasons for non-participation at each stage, if possible. | NA |
| 11c | Report response rate, present the definition of response rate or the formula used to calculate response rate. | 8 |
| 11d | Provide information to define how unique visitors are determined. Report number of unique visitors along with relevant proportions (e.g., view proportion, participation proportion, completion proportion). | 8 |
| Descriptive  results | 12 | Provide characteristics of study participants, as well as information on potential confounders and assessed outcomes. | 8 |
| Main findings | 13a | Give unadjusted estimates and, if applicable, confounder-adjusted estimates along with 95% confidence intervals and p-values. | NA |
| 13b | For multivariable analysis, provide information on the model building process, model fit statistics, and model assumptions (as appropriate). | NA |
| 13c | Provide details about any sensitivity analysis performed. If there are considerable amount of missing data, report sensitivity analyses comparing the results of complete cases with that of the imputed dataset (if possible). | NA |
| **Discussion** | | |  |
| Limitations | 14 | Discuss the limitations of the study, considering sources of potential biases and imprecisions, such as non-representativeness of sample, study design, important uncontrolled confounders. | NA |
| Interpretations | 15 | Give a cautious overall interpretation of results, based on potential biases and imprecisions and suggest areas for future research. | 16,17 |
| Generalizability | 16 | Discuss the external validity of the results. | 16,17 |
| **Other sections** | | |  |
| Role of funding source | 17 | State whether any funding organization has had any roles in the survey’s design, implementation, and analysis. | 17,18 |
| Conflict of interest | 18 | Declare any potential conflict of interest. | 17,18 |
| Acknowledgements | 19 | Provide names of organizations/persons that are acknowledged along with their contribution to the research. | 17,18 |

**Supplementary Table 3. Preliminary statements**

|  |  |
| --- | --- |
| Statements | |
| 1 | Biosimilars are as effective and safe as the originator or tolerability issues. |
| 2 | Biosimilars can be used both in biologic-naïve patients and in patients already treated with the originator drugs. |
| 3 | The main reason for switching from an originator drug to a biosimilar is its lower cost. |
| 4 | Switch from an originator drug to a biosimilar can be performed at any time. |
| 5 | The switch from an originator drug to a biosimilar is effective and safe. |
| 6 | Multiple switches from one biosimilar to another are feasible in case of drug unavailability. |
| 7 | There is no sufficient evidence to support multiple switch in case of loss of response to a biosimilar |
| ~~8~~ | There is no sufficient evidence to support reverse switch to the originator drug |
| 9 | There is no need to monitor drug trough levels and autoantibodies in patients switched from the originator drug to the biosimilar |
| 10 | The non-medical switch is a way to reduce costs associated with advanced therapies and increase accessibility. |
| 11 | In the near future, non-anti-TNF biosimilar drugs are expected to alter the therapeutic algorithm in patients with inflammatory bowel diseases. |