

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This study is a descriptive, observational, retrospective study of secondary data collected between 2011 and 2020 using the DATASUS to characterize ICs in patients with UC. The sample size of this study is huge, including all cases in the Brazilian public health system that met the included criteria for inclusion. The result will help us to understand the clinical progression of ulcerative colitis in Brazil. However, there were three major problems in this study. Firstly, this study is descriptive and lack of analysis, which will greatly reduce the clinical significance. It would be better if this study can conduct case control or cohort study, comparing the effects of different conventional drugs on ICs. Secondly, the definition of IC is not reasonable. The three IC proxies cannot replace all kinds of complications, which will increase the possibility of bias or error. Thirdly, five traditional drugs have been used for patients with ulcerative colitis in the study. Only the total time that a patient was given these conventional medicines was concerned in the study. It would be better if the authors could obtain the time one patient was given a certain traditional drug alone and analyze distribution of intestinal complications under different drugs and different treatment times.

We thank the reviewer for the comments. Observational studies have limitations and we listed all our study limitations in the section before results. We will explain the major problems described by the reviewer in the same order listed:

1. The objective of our study was to describe the real world treatment of ulcerative colitis in the Brazilian public healthcare system, which from 2011 to 2020 relied only in conventional therapies. A comparative study between the different conventional therapies is a good idea. However, it would add

even more limitations due to the characteristics of the administrative database (DATASUS), the lack of clinical data that makes it difficult to balance cohorts. We added a sentence in study design to explain the reasons why this kind of analysis were not conducted.

2. We are aware of the limitations of establishing IC proxies, we expect that there is an underestimation of ICs, which was cited on the discussion section. To minimize the bias and error the initial list of ICs was based on the literature and after that we had 4 independent clinical experts to review and approve the final list.
3. A comparative study would add more limitation to the study due to the administrative database characteristics. We added a new sentence in study design to explain the reasons. The objective of this study was to describe the real world treatment of ulcerative colitis in the Brazilian public healthcare system, which from 2011 to 2020 relied only in conventional therapies.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The author studied the materials related to the routine treatment of ulcerative colitis in Brazil in the past decade. With a large sample size, it systematically describes the general information and treatment prognosis of patients with ulcerative colitis in Brazil, which has certain guiding significance for clinical practice. It involves not only medical content, but also health economics and medical law. The research belongs to retrospective research, which is generally innovative and readable. It is suggested to appropriately reduce the length of the research, simplify some

health economics and legal content involving medical disputes, because the medical policies of different countries are different. To increase readability. It is suggested to review after modification.

We thank the reviewer for taking the time to review our paper. Brazil have indeed very specific medical policies, the objective of our study is to describe the ulcerative colitis treatment in the public healthcare system from 2011 to 2020, that is why we think it is important to understand which treatments were available and how the ICs could be reported in the database. We do provided very detailed information about the methodology, database and analysis in the hope that readers from other countries can understand it. To increase readability we removed database specificities and information related to the public database that does not impact the study.

Reviewer #3:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: 1. Conventional therapy is recommended for patients with mild-to-moderate UC, so, authors should conduct a stratified analysis basing on different severities. 2. Authors should elucidate the reasons for UC flares, like poor compliance with prescribed medicine?

We would like to thank the reviewer. The situation from our study is that there were no other treatment options for ulcerative colitis patients in the public healthcare system besides conventional therapy. Independently of the severity of the disease, that was the only treatment they could get. However, we know that conventional therapy is more suitable for mild UC. Due to the lack of clinical data in the database used for the study we could

not stratify the analysis based on different severities, this limitation was added to the limitations section “The severity of the disease was not considered in the analyses due to methodological limitations.”.

Some reasons for UC flares are mentioned in the discussion, like the use of conventional treatment for severe UC. Treatment compliance was not verify, the patients could combine and change treatment but the main idea was to describe the real world situation in a scenario that patients only have access to conventional therapy. We do mention about how availability of medicines could impact in the treatment in the limitations section “Another limitation refers to the availability of medicines by the SUS, which are not always available and/or are available at different times during the period of this study, such as corticosteroids. Use of conventional therapy was an assumption based on the first claim of each drug at the database, so the patients could have not been under treatment during all the study period.”