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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 69481

Title: Case report of histological remission of eosinophilic esophagitis under asthma therapy with IL-5r monoclonal antibody

Provenance and peer review: Unsolicited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05085577
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Switzerland

Manuscript submission date: 2021-09-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-14 17:17

Reviewer performed review: 2021-10-23 09:55

Review time: 8 Days and 16 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [Y] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Thank you for asking to review the article "Case report of histological remission of eosinophilic esophagitis under asthma therapy with IL-5r monoclonal antibody". The manuscript reports a case report on the remission of EoE under benralizumab treatment for asthma. The topic is rather timely, as a phase 3 trial on Benralizumab for the treatment of EoE is in its final phase. However, I do have some major and minor issues to raise on the contents. Please find attached my comments: Major issue: 1. The paragraph on the description of EoE is somewhat inaccurate, as the authors reported contrasting concepts. Additionally, many sharp considerations are not references. Furthermore, I would recommend carefully reviewing some concepts cited papers for this section. 2. The section "Studies examining IL-5 or IL-5-receptor antagonists in EoE" reports important inaccuracies. There is a phase 3 trial in its final phase for Benralizumab. Minor issues: 1. The authors should add a reference for the Randomised Clinical Trial on Benralizumab in EoE. 2. The authors should add a definition of active / in remission EoE in the introduction of the manuscript. 3. The authors should report any other concomitant medication for this patient (e.g., elimination diet, PPI, systemic steroids), which could have had an impact on the histologic remission. And also comment on this. 4. The authors should report the presence of possible comorbidities. 5. In the "medical history", "pain in the esophagus" should be non-cardiac chest pain 6. The sentence "(in our case 19, resp. 20 in the biopsies of a gastroscopy in 10/2018)." Could be better formulated. 7. There is a paragraph which is unclear in its chronology: "Gastroscopies were performed on 05/2019 and 11/2020, and the histological examination showed the complete absence of eosinophils. Although

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in histological remission, our patient reported pain in the esophagus (both spontaneously and more so after eating food) and food impaction. Our patient met the criteria for EoE, with dysphagia and food impaction and at least 15 eosinophils per high-power field in the esophageal mucosa (in our case 19, resp. 20 in the biopsies of a gastroscopy in 10/2018)." The authors report symptoms despite histological remission (which is not infrequent in EoE), but then report histology criteria for active EoE. 8. The authors report: "This case harbors typical aspects of the complexity of treating EoE and includes a long interval between the initial symptoms and diagnosis, the interaction with other eosinophilic conditions, psychiatric comorbidities or associated symptoms and chronic illnesses and possible new therapeutic approaches." However, there is no mention of psychiatric disorders earlier in the manuscript 9. A reference should be added for "The pathogenesis of EoE is multifactorial and not fully understood. Genetic predisposition, environmental factors (microbiome, breastfeeding, population density) and food antigens play a role" 10. There is a redundancy in the sentences: "Treatment includes both pharmacological and dietary measures. Triggers cannot be identified in every case, and other therapies consist of PPIs and topical steroids". 11. I wonder why a duodenal image has been added to the manuscript.

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Peer-review model: Single blind

Reviewer's code: 02567669
Position: Editorial Board
Academic degree: MD

Professional title: Emeritus Professor

Reviewer's Country/Territory: Germany

Author's Country/Territory: Switzerland

Manuscript submission date: 2021-09-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-11-07 20:31

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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SPECIFIC COMMENTS TO AUTHORS

This is a very interesting case report. It describes a case of a patient with long-lasting asthma and EoE. The standard biological mepolizumab induced neither a clinical esponse nor a decrease in eosinophil count in the esophagus. In contrast, the anti-I-5-receptor antibody reduced eosinophile counts to nearly zero. But: sysmptoms did persist! The authors discuss that food allergy, psychosomatic situation and other predispositions intermingle to induce asthma + EoE. Further studies are needed to clarify whether anti-IL-5 antibodies or anti-IL-5-receptor antibodies rpove to better ameliorate symptoms in asthma and EoE. Obstructive sleep apnoe syndrome may further exacerbate "asthma", reflux disease, and EoE, and should be treated accordingly. Although I'm not a native speaker, I feel that polishing by an experienced native speaker is helpful for this manuscript.

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Reviewer's code: 02155135
Position: Editorial Board
Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Switzerland

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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SPECIFIC COMMENTS TO AUTHORS

This is a case of a EoE patients with a therapy-resistant asthma who was treated with benralizumab achieving histological remission of EoE . Authors describe a clinical vignette: white men, 56 yrs old who suffered from dyspepsia and food impaction at the age of 28. A diagnostic delay of 19 years was observed before the diagnosis of EoE was made in 2012 on the basis of symptoms, endoscopy and histology [Please, describe here all symptoms, endoscopic findings and initial histology with eosinophilic count and the other findings such as microabscesses etc]. In 2013 he began oral topical glucocorticoids [which one? later in the text Authors stated budesonide] The symptoms intensified [which symptoms?], and esophageal strictures were observed. [Then, did he repeat the upper GI endoscopy that showed strictures that were not described one year before?] [Did he undergo PPI treatment and/or six-food elimination diet, these are added later in the text] In the same year there was a diagnosis of asthma [which therapy began for asthma?]. Then, Authors stated " Because of therapy-resistant asthma" Please, which serum eosinophilic count and nitric oxide had? Did he experience asthma relapses, if yes how many and they required hospitalization? the definition of suboptimal control of asthma should be incorporate in this description In my opinion a description of the clinical vignette of this patient that took into account the chronological order of his clinical history is mandatory. The objective improvement of EoE disease under treatment with benralizumab in terms of total depletion of eosinophils in peripheral blood samples as well as in the histological examination might be expected, however there was limited clinical improvement suggesting that targeting eosinophils alone may be insufficient to prevent histological worsening or reduce

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symptoms in EoE. Benralizumab that directly leads to eosinophil apoptosis, is appealing because it limits the chance for the rebound in eosinophils that can occur with agents mainly targeting eosinophil recruitment. Further studies are mandatory.