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Dear Editor,

First of all we would like to thank you for considering the original article “**Role of Mediterranean diet in preventing platinum based gastrointestinal toxicity in gynecolocological malignancies: a single Institution experience**” by Ghisoni E. et al. for consideration of publication in your *World Journal of Clinical Oncology*.

We carefully red your suggestions and addressed all of them using the track-changes function in the edited manuscript file, including the “new” *ARTICLE HIGHLIGHTS* section.

We filled authors contributions, Institutional review and informed consent statements. Of note, we want to highlight that we removed the supportive foundation statement.

References were updated according to Journal’s instructions providing PMID and DOI, when available.

Finally, Figure 1 was uploads as a separate editable file as requested in a ppt format.

Please find below the point per point response to reviewers.

**#Reviewer 1 (code : 03087211)**

#### **SPECIFIC COMMENTS TO AUTHORS**

The work is good up to some extent but may be improved by inclusion of the following suggestions. 1. English should be improved throughout the manuscript. **We carefully re-checked the entire manuscript and corrected typos when necessary.** 2. Quantitative information should be provided in the abstract. **Several statistical and quantitative information are present in the abstract in the results session.** 3. The concussion should be

concise and to the points indicating the application of the work. We believe that, although in a limited number of patients, our work suggested a potential protective role of the Mediterranean diet in preventing GI toxicities which should be further explored ideally in a perspective study. 4. Novelty of the work be established. This is the first non-interventional study which explored the use of the MDSS exploring the potential role of the Mediterranean Diet in preventing GI toxicities in gynecological patients. 5. First paragraph of introduction should describe the general aspect of cancer with citation of following literature. 6. Refs are not updated and the following refs. should be added. The addition of these may improve the quality of this manuscript. Bioorg. & Med. Chem., 21: 3808-3820 (2013).; Polyhedron 56, 134-143 (2013).; Curr. Can. Drug Targets, 11, 131-134 (2011).; Can. Ther., 8: 6-14 (2011).; Med. Chem. Res., 22, 1386-1398 (2013).; Future Med. Chem., 5, 135-146 (2013).; Chirality, 30, 402-406 (2018). A: With refs 1,2 Curr. Drug Target, 16: 711-734 (2015).; Microb. Pathog., 53, 66-73 (2012).; Current Drug Ther, 7: 13-23 (2012).; Med. Chem., 9, 11-21 (2013).; Egypt. Pharm. J., 9: 133-179 (2010).; Future Med. Chem., 5, 961-978 (2013). B: With refs 12,13 RSC Advances 4, 29629-29641 (2014).; Biomed. Chromatogr., 27, 1296-1311 (2013).; Med. Chem. Comm., 8, 1742-1773 (2017).; J. Mol. Liq., 234, 391-402 (2017).; Chem. Pap., 68, 540-552 (2014).; Biointerf. Res. Appl. Chem., 6: 1356-1379 (2016).; RSC Adv., 8, 37905-37914 (2018).; Curr. Med. Chem., 2159-2187 (2016).;

References were updated and PMID and DOI were added as requested.

I WOULD LIKE TO SEE THE REVISED MANUSCRIPT.

**#Reviewer 1 (code : 02445450)**

#### **SPECIFIC COMMENTS TO AUTHORS**

The authors describe MD would reduce chemotherapy-related GI toxicity. If this is proved, MD would accelerate the QOL of patients with advanced gynecological cancers, improving their prognosis. However, it may need further clarification to prove this. #1. Were the patients with preexisting diseases in the stomach, gallbladder, pancreas, liver, intestine, and colon fully eliminated, using the upper endoscopic exam, abdominal ultrasonography, abdominal CT, and colonoscopy? Thank you for the comment. As stated in the methods session "Patients affected by intestinal chronic disease or any other chronic condition which could impact on GI toxicities or who required parenteral nutrition were excluded from the study." Abdominal CT or MRI are routinely performed at diagnosis before

treatment start. Colonoscopy is not included in the Italian guidelines as diagnostic work-up in case of gynecological malignancies, unless indicated by clinical judgement. #2. Was the status of comorbidities and medical history (especially related to GI diseases) evaluated between MDSS-high and MDSS-low groups? Yes, as reported in the methods section “iii) weight; iv) body mass index (BMI); v) smoke and alcohol habits; vii) number of previous lines; viii) nutritional requirements (basal energy expenditure [BEE] and total energy expenditure [TEE]) were evaluated and well balanced between the two groups.

#3. Was gastrointestinal toxicities score after the chemotherapies compared with that before the therapy? Yes, MSSD and PRO-CTCAE were compared to baseline at each timepoint. #4. What is the mechanism which explains the decrease of gastrointestinal toxicities induced by MD? Thank you for your comment. Numerous studies have already demonstrated a relationship between MD adherence and the prevention of cardiovascular diseases and diabetes. In fact, a well-balanced regimen assures the optimal daily nutritional intakes preventing malnutrition but also playing an anti-inflammatory role. Moreover, a speculative role should be hypothesized in modifying the microbioma.

#5. When gastrointestinal toxicities occurred after the chemotherapy, what work-up was performed to make definitive diagnosis? Symptomatic treatment was given to patients. Diagnostic exams are performed only in case of long-lasting or severe toxicities, which was not the case in our patients series.

Once again thank you in advance for consideration of this manuscript.

We look forward to hearing from you soon and to proceed with next steps.

Yours Sincerely,

Giorgio Valabrega