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Paper: “Clinical Significance of DPYD Gene Polymorphism Testing in Colorectal Cancer Patients Receiving FluoropyrimidineBased Chemotherapy: A Single-Center Study in Latvia”

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Peer review:

Reviewer 1: Florjana Rustemi
Albanian University, Albania

Reviewer 2: Lotfi Saeed Bin Dahman
Hadhramout University Hospital at Hadhramout University, Yemen

Reviewer 3: Blinded

ESJ Manuscript Evaluation Form 2026

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Please respond within the appointed time so that we can give the authors timely responses and feedback.

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Reviewer Name: Florjana Rustemi	
University, Country: Albanian University, Albania	
Date Manuscript Received: June 11, 2026	Date Review Report Submitted: June 25, 2026
Manuscript Title: Clinical Significance of DPYD Gene Polymorphism Testing in Colorectal Cancer Patients Receiving Fluoropyrimidine-Based Chemotherapy: A Single-Center Study in Latvia	
ESJ Manuscript Number: 0646/26	
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Evaluation Criteria:

Please give each evaluation item a numeric rating on a 5-point scale, along with a thorough explanation for each point rating.

Questions	Rating Result [Poor] 1-5 [Excellent]
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1. The title is clear, and it is adequate for the content of the article.	5
The title is precise, informative, and accurately reflects the scope and focus of the study. It clearly indicates the clinical context, intervention and study design.	
2. The abstract presents objectives, methods, and results.	5
The abstract is well-structured and comprehensive. It clearly outlines the background, aim, methodology, key findings and conclusions.	
3. There are a few grammatical errors and spelling mistakes in this article.	4
Overall, the manuscript is well-written, in academic tone and it is clear for the readers. Minor mistakes are present, such as formatting inconsistencies like: spacing, punctuation and typing errors.	
4. The study methods are explained clearly.	5
The methods section is detailed, describing study design, inclusion/exclusion criteria, genotyping procedures, toxicity assessment, and statistical methods clearly. The use of separate retrospective and prospective cohorts improves the clarity and reproducibility of the research.	
5. The results are clear and do not contain errors.	5
Results are structured, supported by numerical data and tables. Key outcomes are clearly reported and consistent with the study design.	
6. The conclusions or summary are accurate and supported by the content.	4
The conclusions appropriately reflect the findings without overstating the results. The limitations are acknowledged correctly and the need for larger studies is emphasized by the authors. The link between genotype-guided dosing and potential toxicity reduction is supported by the data presented.	
7. The references are comprehensive and appropriate.	4
References are extensive, mainly up-to-date, except for references no. 9, 13, 14, 16, 23 (which are not up to date) They references support background context and discussion points.	

Overall Recommendation (mark an X with your recommendation) :

Accepted, no revision needed	
Accepted, minor revision needed	X
Return for major revision and resubmission	
Reject	

Comments and Suggestions to the Author(s):

The manuscript is of high scientific quality and addresses a clinically relevant topic in pharmacogenomics and oncology.

Minor editorial revisions are recommended:

- Clarify which chi-square test has been used.
- Clarify whether all patients followed uniform treatment protocols, as this may influence toxicity outcomes.
- Especially in the Discussion part you can find repetition. Some concepts are repeated multiple times.
- Perform minor language correction.
- Insufficient toxicity analysis that may lead towards limited and superficial clinical interpretation.

Reviewer A:

Recommendation: Revisions Required

The TITLE is clear and it is adequate to the content of the article.

Yes, the title of the manuscript is clear, informative, and adequately reflects the scope, content, objectives, and design of the study.

The ABSTRACT clearly presents objectives, methods, results, and conclusions.

Yes, the abstract is well structured and clearly presents the background, aims, methods, results, and conclusions of the study. However, the authors may consider indicating the statistical methods used. Additionally, emphasizing that only two patients carried clinically relevant DPYD variants would help readers better appreciate the limitations related to the small sample size.

There are a few grammatical errors and spelling mistakes in this article.

The manuscript is generally well written; however, it contains a few grammatical errors and minor spelling mistakes. Professional language editing service is recommended to improve the clarity and readability of the manuscript.

The study METHODS are explained clearly.

The Methods section is generally clear and adequately describes the study design, patient population, genotyping procedures, outcome assessment, statistical analysis, and ethical considerations. However, methodological details should be clarified to enhance reproducibility and scientific rigor.

Major comments should be addressed:

1. Study duration: The authors should specify the dates during which patients were recruited and duration of follow-up for both retrospective and prospective cohort.
2. Study population: Details of the study population is not enough. The authors also should indicate whether a formal sample size estimation was performed and why the sample size is small. The authors should describe briefly how colorectal cancer was diagnosed (mention reference). What are severe comorbid conditions that could independently influence chemotherapy-related toxicity?
3. Genotyping assay: The PCR technique used in this study should be described in greater detail, including the specific assay or commercial kit used, primer information (if applicable), instrumentation, and laboratory quality assurance procedures.
4. Dose chemotherapy: The manuscript states that dose modifications were made according to clinical guidelines. The authors should specify which pharmacogenetic guideline (e.g., CPIC or DPWG) was followed and briefly describe the dosing recommendations applied for each DPYD

variant with the reference.

5. Statistical analysis: The statistical methods require additional detail.

6. Ethical approval: The ethics committee, number, and date of the approval should be reported.

7. Limitation: Although the authors acknowledge the small sample size, but they should discuss the potential limitations introduced by the single-center design and the combination of retrospective and prospective cohorts.

Overall, the methodology section is appropriate for the study objectives and generally well presented. However, addressing the above points would improve the transparency, reproducibility, and quality of the manuscript.

6.

The results are clear and do not contain errors.

The results are generally well organized and presents the findings of the study. However, several points should be written to increase the scientific rigor and avoid overinterpretation of the findings.

1. Avoid interpretation in the results section. For example: For example, this finding is consistent with previously reported data, the observed rate of toxicity, this finding suggests a potential protective effect etc., while interpretation and comparison with previous studies should be reserved for the discussion section.

2. Report absolute numbers with percentages (%). For example: Chemotherapy-related toxicity occurred in 20/46 (43.5%) patients, severe toxicity occurred in 6/46 (13.0%) patients. Also reporting confidence intervals alongside percentages and key estimates would strengthen the statistical presentation.

3. Age group analysis: The authors should report the actual number of patients with severe toxicity in each age group rather than only the p-value. Also, since only two patients carried DPYD variants, conclusions regarding genotype-guided dose adjustment should be presented cautiously.

4. Table 1: Consider adding p-values to this table for comparisons between genotype groups or clearly state that statistical comparisons were not performed because of the extremely small number of variant carriers.

Overall, the results should be improved to support the study objectives, more detailed statistical presentation, and greater caution in interpreting findings derived from a very small number of DPYD variant carriers.

The CONCLUSION or summary is accurate and supported by the content.

Yes, the conclusions are clear, concise, and generally supported by the results presented.

However, the conclusion should avoid implying a causal or definitive clinical benefit of genotype-guided dosing, as only two patients carried clinically relevant DPYD variants. The findings should be presented as preliminary and exploratory, emphasizing that they suggest, rather than confirm, the potential clinical utility of pre-treatment DPYD testing. Given the limited sample size and the small number of patients with actionable variants, no definitive conclusions

can be drawn regarding the impact of genotype-guided dosing on treatment safety or clinical outcomes.

The list of REFERENCES is comprehensive and appropriate.

Yes, the references are comprehensive and appropriate.

Please rate the TITLE of this paper.

[Poor] 1-5 [Excellent]

3

Please rate the ABSTRACT of this paper.

[Poor] 1-5 [Excellent]

3

Please rate the LANGUAGE of this paper.

[Poor] 1-5 [Excellent]

3

Please rate the METHODS of this paper.

[Poor] 1-5 [Excellent]

2

Please rate the RESULTS of this paper.

[Poor] 1-5 [Excellent]

2

Please rate the CONCLUSION of this paper.

[Poor] 1-5 [Excellent]

3

Please rate the REFERENCES of this paper.

[Poor] 1-5 [Excellent]

4

Overall Recommendation!!!

Accepted, minor revision needed

Comments and Suggestions to the Author(s):

The manuscript addresses a clinically relevant topic in pharmacogenetics and provides valuable real-world data on the implementation of DPYD genotyping in colorectal cancer patients receiving fluoropyrimidine-based chemotherapy. The study is generally well organized, and the objectives, methodology, and findings are clearly presented. However, several issues should be addressed to strengthen the manuscript:

1. The manuscript contains a few grammatical errors and minor spelling mistakes. Careful English language editing is recommended.
2. The Methods section should provide additional methodological details, including the study period, the genotyping methodology (PCR assay/platform), statistical analysis used, and the ethics approval name, number, and date.
3. The Results section should focus on presenting the findings objectively. Statements comparing the results with previous studies or discussing their clinical implications should be moved to the Discussion section.
4. The current findings should be described as preliminary and exploratory rather than as evidence supporting the clinical effectiveness of genotype-guided dosing.
5. The authors should discuss the limitations of the study in greater detail, particularly the small sample size, the single-center design, and the limited number of DPYD variants analyzed.
6. Reporting absolute numbers together with percentages and, where appropriate, confidence intervals would improve the presentation of the results.

Overall, after addressing these comments, the manuscript would be suitable for publication.