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| Journal Name: | [**Journal of Cancer and Tumor International**](https://journaljcti.com/index.php/JCTI) |
| Manuscript Number: | **Ms\_JCTI\_140755** |
| Title of the Manuscript: | **ENHANCING CANCER TREATMENT: INTEGRATING PHARMACOMETRICS AND PERSONALIZED MEDICINE IN ONCOLOGY** |
| Type of the Article | **Review Article** |

**PART 1: Comments**

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|  | **Reviewer’s comment**  **Artificial Intelligence (AI) generated or assisted review comments are strictly prohibited during peer review.** | **Author’s Feedback** (It is mandatory that authors should write his/her  feedback here) |
| **Please write a few sentences regarding the importance of this manuscript for the scientific community. A minimum of 3-4 sentences may be required for this part.** | This manuscript holds significant importance for the scientific community by comprehensively reviewing the synergistic integration of pharmacometrics and personalized medicine in oncology. It highlights how this combined approach can revolutionise cancer treatment by enabling more precise dosing, predicting patient responses, and minimising adverse effects, ultimately leading to improved patient outcomes. By detailing the underlying principles, cutting-edge computational models, and the crucial role of genomics and biomarkers, the review provides a foundational resource for researchers and clinicians seeking to advance precision oncology.  Furthermore, it underscores the critical need for interdisciplinary collaboration to unlock the full potential of these combined strategies in the fight against cancer. | This manuscript holds significant value for the scientific community by providing a comprehensive synthesis of pharmacometrics and personalized medicine in oncology, an area poised to revolutionize cancer treatment. It highlights how these approaches enable more precise dosing and tailored therapies, ultimately improving patient outcomes across diverse cancer types. The integration of cutting-edge computational models and biomarker-driven strategies offers a foundation for interdisciplinary collaboration, unlocking new potential in the fight against cancer. Furthermore, it serves as a critical resource for researchers and clinicians seeking to advance precision oncology practices. |
| **Is the title of the article suitable?**  **(If not please suggest an alternative title)** | Yes, the title of the article, "ENHANCING CANCER TREATMENT: INTEGRATING PHARMACOMETRICS AND PERSONALIZED MEDICINE IN ONCOLOGY," is highly suitable. | We appreciate the confirmation that the title is appropriate and accurately reflects the content of the manuscript. We believe it effectively captures the manuscript’s focus on advancing cancer care through these integrated approaches and will retain it as is. |
| **Is the abstract of the article comprehensive? Do you suggest the addition (or deletion) of some points in this section? Please write your suggestions here.** | The abstract of the article is comprehensive and well-structured, effectively summarizing the key arguments and scope of the review. It clearly states the problem, introduces the proposed solution (integration of pharmacometrics and personalized medicine), highlights their contributions, and explains how their combination leads to enhanced outcomes. The mention of specific methodologies and data types (multi-omics) further strengthens its comprehensiveness.  A minor addition could make it even more robust by briefly acknowledging the current challenges or future perspectives of this integration. While the full article might delve into these, a hint in the abstract can give the reader a more complete picture of the landscape. Kindly add a sentence or two at the end of the abstract that briefly alludes to the ongoing challenges or future directions. This would provide a more holistic view of the field.  "Despite this promise, successful integration faces challenges such as data standardization, computational complexity, and regulatory hurdles, necessitating ongoing efforts in collaborative research and technological advancements to fully realize its potential in clinical practice."  No deletions required. | Thank you for the thoughtful suggestion to enhance the abstract by addressing the future challenges and perspectives of integrating pharmacometrics and personalized medicine. We agree that it effectively summarizes the key arguments and proposed solutions, including the integration of pharmacometrics and personalized medicine and with the reviewer’s recommendation and will revise the abstract accordingly by including a brief sentence that reflects the ongoing challenges (such as standardization, regulatory hurdles, and integration complexity) and future directions to provide a more holistic view. |
| **Is the manuscript scientifically correct? Please write here.** | Based on a thorough review of the provided text, the manuscript appears to be scientifically correct.  In "Table 1: Overview of Genomic Technologies and Their Applications in Personalized Cancer Treatment," the application for "Pembrolizumab (Keytruda) Targets PD" is incomplete. While "Targets PD" is correct, specifying "Targets PD-1 (Programmed Death-1)" and its application in "Immunotherapy for various cancers" would make it more precise. However, this is a matter of detail, not scientific incorrectness.  The manuscript demonstrates a solid understanding of the scientific principles and current practices in pharmacometrics and personalized medicine within oncology. | We are grateful for the reviewer’s assessment that the manuscript appears scientifically correct based on the provided text. We have reviewed the content, particularly the sections on genomic technologies and their applications in personalized cancer treatment, such as targeting PD-1 (Pembrolizumab) and PD-L1 in immunotherapy. We will ensure all data and interpretations, including those related to pharmacometric modeling, align with current scientific principles and practices to further solidify the manuscript’s accuracy. |
| **Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.** | The references provided within the text are partially sufficient and somewhat recent, but there's room for improvement in both recency and breadth to truly reflect the state-of-the-art in such a rapidly evolving field.  The references in Table 3 range from 2001 to 2020. While a 2020 reference for 5-Fluorouracil is quite recent  within that table, several others are from the early 2010s (e.g., Druker BJ et al., 2001; Zhou J, Xu B, 2013; Dawson SJ et al., 2013; Brahmer JR et al., 2012). For a review article in 2025 (assuming the request implies this is being written now), citing work from 10-20 years ago as primary examples, while foundational, might miss significant recent advancements.  It's good to include foundational papers (like Druker BJ et al. for Gleevec, which was revolutionary), but  more contemporary examples that build on these foundations would strengthen the review.  Many general statements, particularly those with statistics (e.g., "pharmacometric modelling reduced chemotherapy dose adjustments by 30%... According to the American Society of Clinical Oncology (ASCO), pharmacometrics can improve cancer treatment outcomes by 20-30%"), lack specific citations. While these are presented as common knowledge or from reputable organizations, providing the precise source (e.g., a specific ASCO guideline or report, or the *Clinical Pharmacology & Therapeutics* study) would greatly enhance the scientific rigor and verifiability.  Many of the listed references in Table 3 are tied to specific drugs or cancer types (e.g., 5-Fluorouracil, Docetaxel, Trastuzumab, Imatinib). While valuable, a review article might benefit from more high-level review | We sincerely thank the reviewer for their insightful and constructive feedback. We agree that several references, particularly those from the early 2000s and 2010s, while foundational, could be supplemented with more recent literature. Accordingly, we have Replaced outdated citations in Table 3 with more recent peer-reviewed articles and clinical studies published between 2020 and 2024.  Included updated examples that build upon earlier work and reflect current advancements in pharmacometrics-guided oncology treatment.  In addition to retaining foundational studies (such as Druker BJ et al.), we will incorporate newer systematic reviews, and authoritative guidelines (e.g., from ASCO, ESMO, or FDA reports) that highlight current applications and innovations in pharmacometric-guided cancer therapy.  We acknowledge the reviewer’s suggestion to complement drug-specific references with broader insights. To address this, we have expanded the manuscript to include high-level review articles and position papers discussing the systemic integration of pharmacometrics and personalized medicine, beyond individual drug cases. Revised Table 3’s format slightly to reflect both drug-specific insights and broader clinical frameworks where appropriate.  We acknowledge that the initial manuscript only briefly mentioned machine learning and did not include sufficient or up-to-date citations reflecting the rapid advancements in this field. In response, we have significantly revised the manuscript to incorporate recent review articles (2023–2025) discussing precision oncology, AI-driven drug development, in silico pharmacology, and computational modeling.  We agree with the reviewer that the references could be enhanced for recency and sufficiency. will update the manuscript by incorporating recent comprehensive review articles that cover pharmacometrics, personalized medicine, precision oncology, and their integration. Specifically, We will include "Molecular and modular intricacies of precision oncology - Frontiers" (2024) to reflect advancements in genetic profiling, immunophenotyping, transcriptomics, epigenetic analyses, and master protocols like basket, umbrella, and platform trials. Additionally, We will add "Advancing Precision Medicine: A Review of Innovative In Silico Approaches for Drug Development, Clinical Pharmacology and Personalized Healthcare - MDPI" (February 2024) to address in silico approaches, and "Review of Personalized Medicine and Pharmacogenomics of Anti-Cancer Compounds and Natural Products - PMC" (April 2024) to cover AI, multi-omics, and computational drug design, ensuring the references align with the latest trends, challenges, and future directions in the field.  We appreciate the recommendation to cite specific sources for general claims, such as: “Pharmacometric modeling reduced chemotherapy dose adjustments by 30%”, “ASCO claims pharmacometrics can improve outcomes by 20–30%”.  These statements have now been revised and properly supported with verifiable references: For chemotherapy dose adjustments: We have included a recent study from *Clinical Pharmacokinetics* (2023) and a PopPK model-based evaluation of cytotoxic drugs. For the ASCO-related statement: We have cited the relevant ASCO policy statements and reviews as well. We appreciate the recommendation to enhance the manuscript with recent references on AI and machine learning (ML) applications in oncology and pharmacometrics. We agree with the reviewer and will incorporate the following articles to strengthen the content: "Artificial Intelligence-Driven Innovations in Oncology Drug Discovery: Transforming Traditional Pipelines and Enhancing Drug Design - PubMed Central" (July 2025) for its very recent insights on AI in oncology drug discovery; "Artificial Intelligence Advancements in Oncology: A Review of Current Trends and Future Directions - PMC" (April 2025) for its comprehensive coverage of AI in cancer diagnosis, treatment, and management; "Revolutionizing precision oncology: the role of artificial intelligence in personalized pediatric cancer care - Frontiers" (May 2025) for its broader implications in precision oncology, despite its pediatric focus; and "Machine learning in personalized cancer treatment: Implications for global public health - GSC Online Press" (November 2024) for its direct relevance to ML in personalized cancer treatment. These additions will ensure the manuscript reflects the latest advancements and enhances its credibility.  We will explore and include relevant recent high-impact review articles to reflect the latest developments in this area. Additionally, We will ensure that statistical claims are supported by specific citations from the literature to enhance the manuscript’s current and robust engagement with the scientific community. |

papers or consensus guidelines that discuss the *integration* of pharmacometrics and personalized medicine broadly.

The fields of AI and Machine Learning (ML) in oncology and pharmacometrics are exploding. The current

text mentions machine learning in passing but doesn't have deeply recent references specifically for these advancements as they integrate with pharmacometrics.

To enhance both the recency and sufficiency of the references-recent comprehensive review articles that cover the overarching themes of pharmacometrics, personalized medicine, precision oncology, and their integration. These often summarize the latest trends, challenges, and future directions. For example-

"pharmacometrics personalized medicine oncology review 2023 2024," "precision oncology review latest advancements," "model-informed drug development oncology review."

**"Molecular and modular intricacies of precision oncology - Frontiers" (2024):** This article discusses genetic profiling, immunophenotyping, transcriptomics, and epigenetic analyses, and touches on master protocols like basket, umbrella, and platform trials, which are highly relevant to personalized medicine.

**"Advancing Precision Medicine: A Review of Innovative In Silico Approaches for Drug Development,**

**Clinical Pharmacology and Personalized Healthcare - MDPI" (Feb 2024):** Directly addresses in silico approaches and precision medicine.

**"Review of Personalized Medicine and Pharmacogenomics of Anti-Cancer Compounds and Natural Products - PMC" (April 2024):** Covers personalized treatment strategies including AI, multi-omics, and computational drug design.

For statements like "pharmacometric modelling reduced chemotherapy dose adjustments by 30% in cancer patients," find and cite the original study or report. Similarly, for the ASCO claim. This builds credibility.

Given the rapid advancements, adding more specific and recent references focusing on AI/ML applications would be crucial, especially since the article highlights "computational modeling" as a core component.

"AI in pharmacometrics oncology," "machine learning personalized oncology drug response," "deep learning cancer treatment optimization."

**"Artificial Intelligence-Driven Innovations in Oncology Drug Discovery: Transforming Traditional Pipelines and Enhancing Drug Design - PubMed Central" (July 2025):** Very recent, specifically on AI in oncology drug discovery.

**"Artificial Intelligence Advancements in Oncology: A Review of Current Trends and Future Directions - PMC" (April 2025):** Covers AI in cancer diagnosis, treatment, and management.

**"Revolutionizing precision oncology: the role of artificial intelligence in personalized pediatric cancer care**

**- Frontiers" (May 2025):** While pediatric-focused, it has broader implications for AI in precision oncology. **"Machine learning in personalized cancer treatment: Implications for global public health - GSC Online Press" (Nov 2024):** Directly addresses machine learning in personalized cancer treatment.

While the software is well-covered, recent methodological advancements or case studies using PopPK/PD in complex oncology scenarios (e.g., immunotherapies, ADCs) would be valuable. By incorporating more recent high-impact review articles and specific citations for statistical claims, the manuscript will demonstrate a more current and robust engagement with the scientific literature.

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| **Is the language/English quality of the article suitable for scholarly communications?** | The language and English quality of the article are generally suitable for scholarly communications, but there are several areas where minor refinements could significantly enhance its professionalism, clarity, and flow.  Areas for Improvement (with examples and suggestions):  In the abstract and introduction, "Pharmacometrics, the science of quantitative drug modelling" is repeated. Vary phrasing or combine sentences to avoid repetition once a concept has been introduced.  "Pharmacometrics, the science of quantitative drug modelling, has emerged as a vital tool in optimizing cancer therapy. By leveraging advanced statistical and computational methods, it enables the development of personalized treatment plans..." (Here, "it" replaces the repeated phrase).  Minor grammatical mistakes are present. | Thank you for the constructive feedback. We agree that the language and English quality of the article are generally suitable for scholarly communications, and we will address the suggested improvements. We will vary the phrasing in the abstract and introduction by combining sentences and replacing repetitive phrases, such as rewording "Pharmacometrics, the science of quantitative drug modelling" and using "it" to avoid redundancy, as demonstrated in the example provided. Additionally, We will carefully review and correct the minor grammatical mistakes to enhance the manuscript’s professionalism, clarity, and flow. |
| **Optional/General** comments |  |  |

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| **PART 2:** | | |
|  | **Reviewer’s comment** | **Author’s comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)* |
| **Are there ethical issues in this manuscript?** | *(If yes, Kindly please write down the ethical issues here in details)* | As this is a review article based entirely on existing literature, no ethical approval was required and we confirm there are no ethical issues in the manuscript. |