

Peer Review File

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Reviewer A

This study addresses a current topic.

The manuscript is quite well written and organized.

Figures and tables are comprehensive and clear.

The introduction explains in a clear and coherent manner the background of this study.

We suggest the following modifications:

Comment1: Introduction section: although the authors correctly included important papers in this setting, we believe the evolving systemic treatment scenario for breast tumors should be further discussed and some recent papers added within the introduction (PMID: 35378995; PMID: 38100933; PMID: 39518127; PMID: 38595817; PMID: 37819422), only for a matter of consistency. We think it might be useful to introduce the topic of this interesting study.

Answer: Thank you for your suggestion. We have added these citations where appropriate in the manuscript (lines 585-605).

Changes in the text:

3. Rizzo A, Cusmai A, Acquafredda S, et al. KEYNOTE-522, IMpassion031 and GeparNUEVO: changing the paradigm of neoadjuvant immune checkpoint inhibitors in early triple-negative breast cancer. *Future Oncol.* 2022;18(18):2301-2309. doi:10.2217/fon-2021-1647
4. Rizzo A, Schipilliti FM, Di Costanzo F, et al. Discontinuation rate and serious adverse events of chemoimmunotherapy as neoadjuvant treatment for triple-negative breast cancer: a systematic review and meta-analysis. *ESMO Open.* 2023;8(6):102198. doi:10.1016/j.esmoop.2023.102198
5. Sahin TK, Ayasun R, Rizzo A, Guven DC. Prognostic Value of Neutrophil-to-Eosinophil Ratio (NER) in Cancer: A Systematic Review and Meta-Analysis. *Cancers (Basel).* 2024;16(21):3689. Published 2024 Oct 31. doi:10.3390/cancers16213689
6. Caputo R, Buono G, Piezzo M, et al. Sacituzumab Govitecan for the treatment of advanced triple negative breast cancer patients: a multi-center real-world analysis. *Front Oncol.* 2024;14:1362641. Published 2024 Mar 26. doi:10.3389/fonc.2024.1362641
- 2.7. Guven DC, Erul E, Kaygusuz Y, et al. Immune checkpoint inhibitor-related hearing loss: a systematic review and analysis of individual patient data. *Support Care Cancer.* 2023;31(12):624. Published 2023 Oct 11. doi:10.1007/s00520-023-08083-w

Comment2: Methods and Statistical Analysis: nothing to add.

Answer: Thank you for recognizing our work.

Changes in the text: None

Comment3: Discussion section: Very interesting and timely discussion. Of note, the authors should expand the Discussion section, including a more personal perspective to reflect on. For example, they could answer the following questions – in order to facilitate the understanding of this complex topic to readers: what potential does this study hold? What are the knowledge gaps and how do researchers tackle them? How do you see this area unfolding in the next 5 years? We think it would be extremely interesting for the readers.

Answer: Thank you for your precious comments and advice. We have added a discussion of the difficulties of future applications and development of this research to the discussion section of the manuscript (lines 542-547).

Changes in the text: It is critical to work closely with clinical experts to refine and standardize the process so as to improve the clinical applicability and ease of use. In addition, the retrospective nature of the recruitment of patients with BRCA might have affected results. In the future, more cost-effective genetic tests will bring more universal convenience to the research of this technology. This technology, combined with the judgement of clinicians, will provide patients with personalized guidance for diagnosis and treatment.

Comment 4: However, we think the authors should be acknowledged for their work. In fact, they correctly addressed an important topic, the methods sound good and their discussion is well balanced.

One additional little flaw: the authors could better explain the limitations of their work, in the last part of the Discussion.

Reply: Thank you for the correction. The comment is similar to comment3, and together we have added the limitations of the study to the discussion.

Changes in the text: None.

Comment 5: We believe this article is suitable for publication in the journal although major revisions are needed. The main strengths of this paper are that it addresses an interesting and very timely question and provides a clear answer, with some limitations.

We suggest a linguistic revision and the addition of some references for a matter of consistency. Moreover, the authors should better clarify some points. The authors should better clarify some points.

Reply: Consistent with the above COMMENT, we added this point to the discussion together.

Changes in the text: None.

Reviewer B

1. The authors mentioned “**studies...**”, while only one reference was cited. Change “Studies” to “A study” or add more citations. Please revise.

Studies have shown that patients with a higher TMB may benefit from ICI therapy 错误!未找到引用源。 .

Answer: We have added changes to the manuscript as you requested (line 294).

2. Please explain their meaning in the legend.

1) Fig 1

*, **, ***

2) Fig 2

, **, ns

3) Fig 3

*, **, ***, ****, ns

4) Fig 6

*, ***, ****, ns

5) Fig 7

*, **, ***, ****, ns

6) Fig 8

7) Fig S2

*, **, ***

8) Fig S3

, *

9) Fig S4

*, **, ****, ns

Answer: We note the significance of these signs in the figure legend.

3. Fig S1

Please provide the unit



Answer: We indicate the unit of Age.

4. Figure S3A-3F

- 1) The legend of Figure S3B is missing
- 2) No Figure S3G, while there is Figure S3G in the legend

Answer: We have changed these errors (line 828-830).