IOCD 2025 Conference

The 1st International Online Conference on Diseases

09–11 September 2025 | Online

MDPI

CD47-targeted therapies in breast cancer treatment: a systematic review of preclinical- and early-phase clinical studies

Mohammad-Salar Hosseini[1,2,3*], Farhad Jadidi-Niaragh[4*], Sarvin Sanaie[2,3], Ata Mahmoodpoor[2,5]

[1]Hematology and Oncology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
[2]Research Center for Integrative Medicine in Aging, Aging Research Institute, Tabriz University of Medical Sciences, Tabriz, Iran
[3]Iranian Cancer Control Center (MACSA) – Tabriz Branch, Tabriz, Iran
[4]Department of Immunology, Immunology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
[5]Department of Anesthesiology and Critical Care Medicine, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

INTRODUCTION & AIM

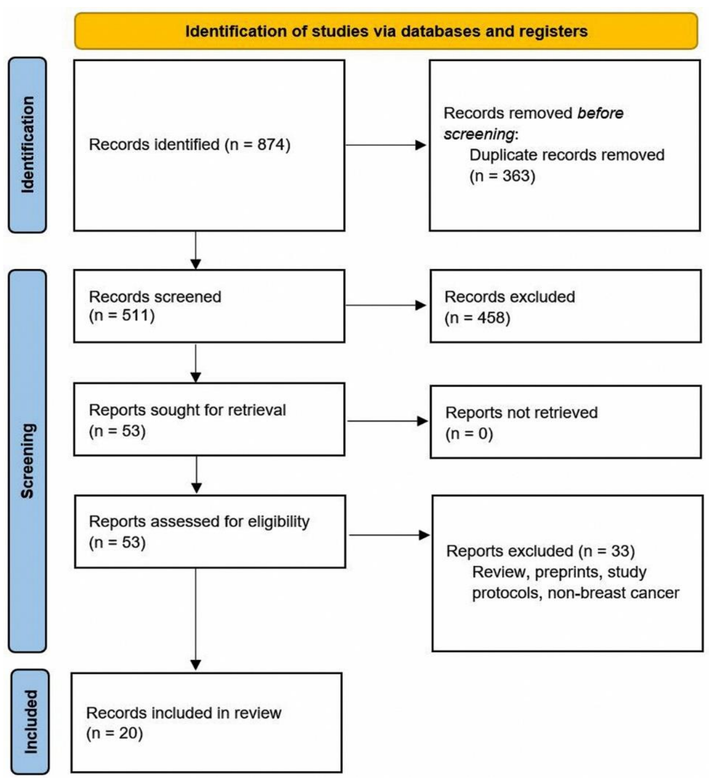
CD47 has emerged as a significant therapeutic target in breast cancer (BC) treatment due to its role in immune evasion, with recent studies suggesting enhanced macrophage phagocytic activity through CD47 blockade. This study aims to provide a secondary analysis of CD47 blockade in the treatment of BC.

METHOD

Following the PRISMA2020 guidelines, Medline (via PubMed), Web of Science, and Scopus were systematically searched using keywords and MeSH terms representing CD47, integrin-associated protein, thrombospondin-1, SIRPα, BC, and their equivalents. The results were screened, and irrelevant studies, preprints, review articles, and studies focusing solely on other tumors, secondary BC, or BC metastases were removed.

RESULTS & DISCUSSION

From the 874 screened records, 20 records were finally included. Studies reported CD47 blockade using various agents, including Hu5F9-G4, MIAP301, MIAP410, and B6H12 antibodies; anti-CD47 siRNA nanoparticles; and tumor vaccines loaded with CD47-targeting agents. Most studies reported the combination of CD47 blockade with other treatment modalities. All studies reporting the dual blockade of CD47 and HER2 using trastuzumab showed significant synergistic effects. CD47-targeting regimens demonstrate their effectiveness through the regulation of cAMP, the suppression of EGF signaling pathways, and an effect on the tumor microenvironment through M2 macrophages and regulatory T-cell depletion, resulting in the activation of an antitumor innate immune response, improved antitumor responses, and a reduction in tumor growth and proliferation, especially in triple-negative BC. So far, the dual CD47/HER2-targeting IMM2902 has shown significant antitumor effects, along with acceptable safety and tolerability.



CONCLUSION

CD47 targeting is a promising anticancer approach to BC. The optimum effects of CD47 blockade are mostly observed when it is administered in combination with other treatment modalities. Specifically, CD47 blockade has shown potential in the treatment of HER2+ BC—regardless of whether the tumor is trastuzumab-resistant or -sensitive. Future studies are required to evaluate its effectiveness in terms of its statistical significance, the optimum combination therapy regimens, and the treatment toxicities.

FUTURE WORK / REFERENCES

1.van Duijn A. et al., Cancer.2022;10:e004589. **2.**Betancur, P. et al., Nat Commun.2017;8:14802. **3.**Page MJ. et al., BMJ.2021;372:n71. **4.**Manna PP. and Frazier WA., Cancer Res.2004;64:1026-1036. **5.**Bener GA., et al., BMC Immunol.2016;17(1):32. **6.**Kaur S. et al., Oncotarget.2016;7(9):10133-10152. **7.**Feliz-Mosquea YR. et al., Breast Cancer Res Treat.2018;172(1):69-82. **8.**Noman MZ. et al., Oncoimmunology.2018;7(4):e1345415. **9.**Iribarren K. et al., Oncoimmunology.2019;8(3):1550619. **10.**Tsao LC. et al., JCI Insight.2019;4(24). **11.**Candas-Green D. et al., Nat Commun.2020;11(1):4591. **12.**Billerhart M. et al., Mol Ther Oncolytics.2021;23:192-204. **13.**Cao X. et al., J Immunother Cancer.2021;9(3). **14.**Kosaka A. et al., J Exp Med.2021;218(11). **15.**Upton R. et al., Proc Natl Acad Sci U S A.2021;118(29). **16.**Bian Y. et al., Biomedicines.2022;10(8). **17.**Li L. et al., Cell Mol Life Sci.2022;79(2):83. **18.**Li Y. et al., Biomater Sci.2022;10(23):6755-6767. **19.**Zhang B. et al., Front Oncol.2022;12:897561. **20.**Li S. et al., Front Pharmacol.2023;14:1142374. **21.**Kaur S. et al., Front Cell Dev Biol.2024;12:1356421. **22.**Tong S. et al., Int Immunopharmacol.2024;130:111708. **23.**Zhang B. et al., Drug Resist Updat.2024;74:101068.

***Corresponding authors** at hosseinim@tbzmed.ac.ir and jadidif@tbzmed.ac.ir.