Clinical Medicine and Medical Research
Received 10 Dec 2020 | Revised 20 Jan 2021 | Accepted 25 Jan 2021 | Published Online 31 Jan 2021

CMMR 02 (01), 65–69 (2021)

ISSN (O) 2693-499X

RESEARCH ARTICLE

Immunotherapy For Advanced Breast Cancer, An Overview Study

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Abstract

An elevated risk of breast cancer is related to the history of illness in individuals or families, and hereditary gene defects in the susceptibility genes to breast cancer. Since 2019, two breast cancer immunotherapies have been approved. Individuals with triple-negative breast cancer can benefit more from immunotherapy than individuals with other breast cancer types. A woman has successfully healed with late stage breast cancer and this is attributed to her own immune system. Researchers produced cells in a programmed process of cell death called necroptosis. These died cells order the immune system to assault and destroy the cells of the body. ***Conclusions:*** Immunotherapy is indicated to finally play its part in the process of treatment of breast cancer. There are several clinical studies in this situation which currently evaluate various immunotherapy forms and combinations. Breast cancer may become a chronic condition easily curable.

Keywords: Breast, Cancer, checkpoints, immunotherapy.

1 | INTRODUCTION

1.1 | Immunotherapy:

An elevated risk of breast cancer is related to the history of illness in individuals or families, and hereditary gene defects in the susceptibility genes to breast cancer. BRCA1 and BRCA2 and other rare genetic gene variants are included. A hereditary predisposition to breast cancer accounts for around 5% to 10% of all cases of breast cancer, but is uncommon in the general population (less than 1%) [1]. The risk to develop breast cancer for women with mutations of BRCA1 and BRCA2 is projected at 45% to 65% by age 70, but at age 40, the risk is higher. People with such mutations should speak to a genetic counselor about their dangers. Other recognized risk factors include obesity, use of hormonal therapy (MHT), high breast density and alcoholic drinking, and physical inactivity [2].

Supplementary information The online version of this article (https://doi.org/xx.xxx/xxx.xx) contains supplementary material, which is available to authorized users.

For certain forms and stages of breast cancer there is a reasonably wide variety of therapies other than immunotherapy. Since 2019, two breast cancer immunotherapies have been approved [3]. The first is atezolizumab (Tecentriq) and paclitaxel (Abraxane) for advanced local triple negative breast cancer which cannot be eliminated by surgery and triple negative breast metastatic cancer. Breast cancers whose positive test for the PD-L1 protein are only approved for treatment by Atezolizumab. A single therapy is approved for the treatment of metastatic cancer and/or cancer which cannot be eliminated by surgery with a molecular modification known as an MSI-H or an MSI-H deficiency (dMMR) [4, 5].

Researchers are beginning to get scientific clues about who is most likely to help with immunotherapy. For instance, individuals with triple-negative breast cancer can benefit more from immunotherapy than individuals with other breast cancer types. In women with elevated gene mutations in their breast cancer or with higher protein levels called PD-L1 tumor cells, immunotherapy may be more successful. There is also some evidence showing that immunotherapy will function well if it is performed early during therapy [6].

Immunotherapy can cause serious, life threatening, side-effects. Heart and blistering responds and flu-loving symptoms such as fever, fatigue, faintheartedness and body aches are the most frequent side effects of immunotherapy. Various forms of immunotherapy can cause various adverse reactions. The high cost of this care that insurance providers are unable to afford is a big third obstacle [7].

2 | IMMUNE CHECKPOINT INHIBITORS:

The immune system needs to be able to discern the difference between cells or compounds that are ”self” (part of you) compared with ”non-self” in order to initiate the immune system reaction to a foreign invader (not part of you and possibly harmful). The cells of the body have proteins on or within their surface that make the immune system recognize them as ”self”. Any of these proteins that promote the identification of ”self” cells in the immune system are called immune checkpoints [8]. Cancer cells often discover ways of using these immune checkpoints to prevent the immune system from being detected and targeted. Any of these proteins that facilitate ”self” cell recognition in the immune system are referred to as immune controls [9]. Cancer cells also find means of utilizing immune proteins in order to avoid the identification and targeting of the immune system. The inhibitors of immune checkpoints target certain immune control proteins which help to recognize and attack cells. Immune checkpoints. Immune checkpoints inhibitors primarily strip the brakes from the immune system by blocking the cancer cell or T cell inhibitor proteins that react to them [10,11].

In March 2019, the FDA approved a triple-negative metastatic breast Cancer checkpoint inhibitor drug for patients whose cancers express the protein of atezezolizumab (Tecentriq), the first anti-PD-L1 antibody receptor, named atezolizumab (Tecentriq®), in conjunction with chemotherapy [12].

3 | A WOMAN SUCCESSFULLY TREATED BREAST CANCER IN LATE STAGE:

Since chemotherapy has failed, a woman has successfully healed with late stage breast cancer and this is attributed to her own immune system. Our immune system is like a custom assassin. With 99,999 percent specificity, it detects and kills something alien in the body. The remainder of 0.01% could be small, but lethal. Cancer cells are, for example, dangerously mutated cells that cannot be detected or killed by the immune system [13].

A method of cell camouflage used by cancerous cells instills the immune system into seeing it as normal cells. Now, before it can kill us, we might have a way to do something and kill cancer. In order to clear this camouflage, researchers have created an immune treatment. The therapy works like a bait that tricks the immune system into recognizing cancer cells as old dying cells. The loss of cells is a normal body process, and dying cells will cause the immune system’s activation. Researchers produced cells in a programmed process of cell death called necroptosis. These died cells order the immune system to assault

and destroy the cells of the body. This approach was tested by injecting these dead cells into the mouse tumors and finding the immune cells killer to invade the cancer and delay its development. This is not the only trick scientists have discovered. Another technique for inducing nectroptosis inside tumor cells themselves was created instead of injecting moving cells. The gene was used to infect the tumor cells by the virus for a necroptosis-triggering enzyme. It also helped to destroy the tumors by the immune system. In contrast with traditional chemotherapy, this method of treatment has many benefits [13, 14].

Immunotherapy increases target identification and kills cancer cells with usually less side effects from the immune system. This makes for longer stretches of administration. It can also be used without adding toxicity in conjunction with other agents. In another pioneering study, the researchers used patient's own immune cells to battle cancer and cured a woman with metastatic breast cancer in an advanced stage. Genetic mutations in normal cells can lead to cancer, which leads to the growth of these cells out of control [15]. The researchers have identified the cells that are best used to identify these genetic variations and battle cancer from the immune system of the patient. The carefully chosen immune cells are then cultivated with the trillions in the lab and inserted into the bloodstream of the patient. The army has been targeting and destroying cancer cells through advanced immune cells. The breast cancer of the woman vanished completely after the operation [16].

The patient is already cancer-free after almost three years. It is not necessarily irreversible, but it is always efficacious. If anyone cell of the cancer survives, the mechanism of tumor forming will start to replicate again and again. This is the first time a woman has been successfully treated for late stage breast cancer with immunotherapy [17].

The purpose of immunotherapy is to prepare the immune system to pursue the last cancer cells, including those in chemical-resistant metastatic tumors, and kill them. The immune system's capacity to concurrently attack several cancer antigens and respond to shifting cancer cells allows patients less likely to become resistant against immunotherapy. We have secret weapons in our immune system's cancer arsenal. We are not near to mastering all the cancer control capacities of the immune system, but improvement is made. We can see that immunotherapy can win the war on cancer if things proceed in this direction [18, 19].

4 | CONCLUSIONS:

In the process of treatment of breast cancer, immunotherapy is indicated to finally play its part. There are several clinical studies in this situation which currently evaluate various immunotherapy forms and combinations. The dynamic connection between the host, the tumor and the common microenvironnement between the two must also be better understood. We must also emphasize the identification of the biomarkers that will direct therapy in suitable patients in this period of ultragenomic research. Finally, we must redefine new endpoints that represent a survival advantage that could vary significantly from one patient to the next. Immunotherapy transforms the world of cancer in ways that we have not imagined before. Breast cancer may become a chronic condition easily curable as well as preventable by customizing immunotherapy to both the disease and the woman.

5 | REFERENCES

1. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: breast cancer. Natl Compr Cancer Netw. 2017. doi:10.1016/j.amepre.2011.02.015.

2. Robson M, Im S-A, Senkus E, et al. Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. N Engl J Med. 2017; 377:523–533. doi:10.1056/NEJMoa1706450.

3. Domingues B, Lopes J, Soares P, Populo H. Melanoma treatment in review. ImmunoTargets Ther. 2018; 7:35–49. doi:10.2147/itt.s134842.

4. Mok TSK, Wu YL, Kudaba I, et al. Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally

advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): a randomised, open-label, controlled, phase 3 trial. Lancet. 2019; 393:1819–1830. doi:10.1016/S0140-6736(18)32409-7.

5. Adams S, Loi S, Toppmeyer D, et al. Phase 2 study of pembrolizumab as first-line therapy for PD-L1–positive metastatic triple-negative breast cancer (mTNBC): preliminary data from KEYNOTE-086 cohort B. J Clin Oncol. 2017. doi:10.1200/jco.2017.35.15_suppl.1088.

6. Adams S, Schmid P, Rugo HS, et al. Pembrolizumab monotherapy for previously treated metastatic triple-negative breast cancer: cohort A of the phase II KEYNOTE-086 study. Ann Oncol. 2019. doi:10.1093/annonc/mdy517.

7. Schmid P, Adams S, Rugo HS, et al. Atezolizumab and nab-paclitaxel in advanced triple-negative breast cancer. N Engl J Med. 2018; 379:2108–2121. doi:10.1056/NEJMoa1809615.

8. Havel JJ, Chowell D, Chan TA. The evolving landscape of biomarkers for checkpoint inhibitor immunotherapy. Nat Rev Cancer. 2019; 19:133–150. doi:10.1038/s41568-019-0116-x.

9. Duffy MJ, Crown J. Biomarkers for predicting response to immunotherapy with immune checkpoint inhibitors in cancer patients. Clin Chem. 2019; 65:1228–1238. doi:10.1373/clinchem.2019.303644.

10. Force J, Leal JH, McArthur HL. Checkpoint blockade strategies in the treatment of breast cancer: where we are and where we are heading. Curr Treat Options Oncol. 2019 Mar 28;20(4):35.

11. Kwa MJ, Adams S. Checkpoint inhibitors in triple-negative breast cancer (TNBC): where to go from here. Cancer. 2018; 124:2086–2103. doi:10.1002/cncr.31272

12. Nanda R, Chow LQM, and Dees EC, et al. Pembrolizumab in patients with advanced triple-negative breast cancer: phase Ib keynote-012 study. J Clin Oncol. 2016; 34:2460–2467. doi:10.1200/JCO.2015.64.8931.

13. Adams S, Gatti-Mays ME, Kalinsky K, et al. Current landscape of immunotherapy in breast cancer: a review. JAMA Oncol. 2019; 5:1205. doi:10.1001/jamaoncol.2018.7147.

14. Sambi M, Bagheri L, Szewczuk MR. Current challenges in cancer immunotherapy: multimodal approaches to improve efficacy and patient response rates. J Oncol. 2019; 2019:1–12. doi:10.1155/2019/4508794.

15. Schmid P, Salgado R, Park YH, Muñoz-Couselo E, Kim SB, Sohn J, et al. Pembrolizumab plus chemotherapy as neoadjuvant treatment of high-risk, early-stage triple-negative breast cancer: results from the phase 1b open-label, multicohort KEYNOTE-173 study. Ann Oncol. 2020 May; 31(5):569–81.

16. Schmid P, Cortes J, Pusztai L, McArthur H, Kümmel S, Bergh J, et al.; KEYNOTE-522 Investigators. Pembrolizumab for Early Triple-Negative Breast Cancer. N Engl J Med. 2020 Feb; 382(9):810–21.

17. Loi S, Giobbie-Hurder A, Gombos A, Bachelot T, Hui R, Curigliano G, et al.; International Breast Cancer Study Group; Breast International Group. Pembrolizumab plus trastuzumab in trastuzumab-resistant, advanced, HER2-positive breast cancer (PANACEA): a single-arm, multicentre, phase 1b-2 trial. Lancet Oncol. 2019 Mar; 20(3):371–82.

18. Loi S, Giobbie-Hurder A, Gombos A, Bachelot T, Hui R, Curigliano G, et al.; International Breast Cancer Study Group; Breast International Group. Pembrolizumab plus trastuzumab in trastuzumab-resistant, advanced, HER2-positive breast cancer (PANACEA): a single-arm, multicentre, phase 1b-2 trial. Lancet Oncol. 2019 Mar; 20(3):371–82.

19. Shen J, Zhao W, Ju Z, Wang L, Peng Y, Labrie M, et al. PARPI triggers the STING-dependent immune response and enhances the therapeutic

efficacy of immune checkpoint blockade independent of BRCANEss. Cancer Res. 2019 Jan;79(2):311–9.

How to cite this article: A.A.D. **Immunotherapy For Advanced Breast Cancer, An Overview Study**. Clinical Medicine and Medical Research. 2021;65−69. https://doi.org/xx.xxx/xxx.xx