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Unlocking precision oncology: the role of neoantigen-based cancer vaccines

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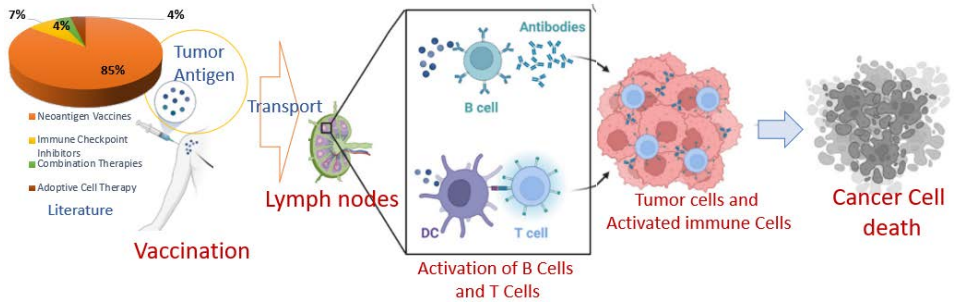
ABSTRACT



Neoantigen-based cancer vaccines represent an innovative and promising approach in precision oncology, using tumor-specific mutations to create tailored immune responses against cancer. These vaccines have shown considerable potential in recent clinical trials, demonstrating safety, feasibility, and the ability to elicit strong immune activity with promising clinical outcomes across various cancer types. This review explores the latest advancements in neoantigen-based vaccines, their current challenges, and the future strategies needed to integrate these vaccines into mainstream cancer treatment, emphasizing their transformative potential in advancing personalized medicine. Clinical trials have demonstrated their safety and feasibility, with results showing robust immune activation, including the generation of neoantigen-specific CD4+ and CD8+ T cell responses, and clinical benefits such as prolonged progression-free survival and tumor regression in some patients. Despite these successes, challenges such as tumor heterogeneity, variability in immune responses, and immune evasion mechanisms remain barriers to widespread implementation. Combining neoantigen vaccines with other therapies, such as checkpoint inhibitors or adoptive T cell therapies, has shown potential to overcome these issues.

Keywords: Neoantigen-based cancer vaccines, Precision oncology, Tumor-specific mutations, Personalized immunotherapy

INTRODUCTION

Neoantigens are unique, tumor-specific antigens produced as a direct result of somatic mutations in cancer cells, leading to the expression of abnormal proteins that are absent in normal tissues. These mutated proteins are processed within the cancer cell and broken down into smaller peptide fragments(1). These fragments are then loaded onto major histocompatibility complex (MHC) molecules—specifically MHC class I for cytotoxic T cell activation and MHC class II for helper T cell activation (2). Once presented on the surface of the tumor cells by MHC molecules, neoantigens are recognized as "non-self" by the immune system, particularly cytotoxic T lymphocytes (CTLs) (3). This recognition triggers an immune response where CTLs bind to the neoantigen-MHC complex on the tumor cells and release cytotoxic molecules like perforins and granzymes, leading to apoptosis or cell death(4). The represenation of action of cancer vaccine is shown in Figure 1. One of the most significant advantages of neoantigens is their specificity to the tumor, which minimizes off-target effects and ensures safer therapeutic interventions(5). Neoantigens have become a cornerstone of personalized cancer immunotherapy, with applications in several innovative approaches(6).

Neoantigen-based vaccines are designed to stimulate an immune response by exposing the immune system to tumor-specific neoantigens(7). Adoptive T cell therapies, such as tumor-infiltrating lymphocytes (TILs) or genetically engineered T cells expressing tumor-specific T-cell receptors (TCRs), focus on enhancing T-cell recognition and destruction of neoantigen-presenting tumor cells(8). Additionally, immune checkpoint inhibitors can indirectly amplify the immune response to neoantigens by relieving inhibitory signals that suppress T-cell activity in the tumor microenvironment(9). Neoantigens are also critical in addressing challenges such as tumor resistance to conventional treatments(11). By targeting tumor-specific mutations, neoantigen-based therapies can overcome the

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limitations of treatments like chemotherapy and radiation, which may fail due to genetic variability and tumor adaptation(12). Furthermore, neoantigens offer the potential for long-term immune surveillance by stimulating memory T cells, reducing the risk of cancer recurrence(13).

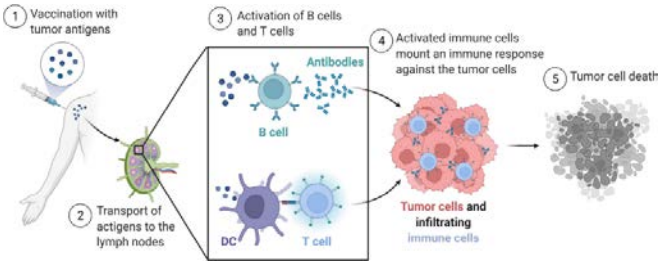

Figure 1. Process of creating a cancer vaccine, where cancer cells are extracted from a patient and broken down into their components. These components are then mixed with an adjuvant to produce a vaccine. Once administered, the vaccine stimulates the patient's immune system to recognize and respond to the cancer's antigens and neoantigens, effectively training the immune system to target and attack the cancer cells. This process aims to boost the body's natural defense mechanisms to fight cancer more effectively. (10)

However, several challenges remain in leveraging neoantigens fully. Tumor heterogeneity, where different regions of a tumor or metastatic sites may have distinct mutational profiles, complicates neoantigen identification and targeting(14). The variability in MHC presentation across patients also poses a hurdle, as not all neoantigens are effectively presented or recognized by the immune system(15). Additionally, tumors can develop immune evasion mechanisms, such as downregulating MHC expression or creating an immunosuppressive microenvironment, which can limit the efficacy of neoantigen-based therapies (16). Despite these challenges, neoantigens hold immense promise as a foundation for next-generation cancer immunotherapies, their ability to elicit strong, specific, and personalized immune responses positions them as a key component in the fight against cancer, with ongoing research aiming to refine their identification, enhance their immunogenicity, and overcome barriers to their clinical application(17). This review aims to explore the latest advancements in identifying and utilizing neoantigens for cancer immunotherapy, examine the key challenges faced in bringing them into clinical practice, and outline potential future strategies to improve their effectiveness and integration into personalized treatments.

METHODOLOGY

The authors explored the role of neoantigen-based cancer vaccines in precision oncology by focusing on clinical trials published between 2019 and 2024 in the PubMed database. A structured query was developed, incorporating MeSH terms and keywords such as "neoantigens," "cancer vaccines," and "clinical trials," applied for publication types and dates. Clinical trials specifically investigating neoantigen-based vaccines for cancer treatment, emphasizing precision oncology strategies were included. Non-clinical studies, review articles, and trials unrelated to neoantigen vaccines were excluded. Data were extracted from the selected studies, including trial identifiers, titles, publication years, cancer types targeted, and outcomes such as safety, efficacy, immune responses, and survival benefits.

DISCUSSION

In their 2023 study, Rojas et.al.(18) explored the potential of personalized RNA neoantigen vaccines to stimulate immune responses in pancreatic ductal adenocarcinoma (PDAC). The Phase I trial involved 19 patients with resected PDAC, from whom tumor samples were analyzed to identify patient-specific mutations (neoantigens). Based on this information, individualized mRNA vaccines encoding up to 20 neoantigens were developed and administered alongside atezolizumab, an immune checkpoint inhibitor, followed by chemotherapy. Of the 16 patients who completed vaccination, 8 showed strong T cell responses targeting their tumor mutations, which correlated with longer recurrence-free survival. At 18 months, none of the responders had cancer recurrence, while non-responders experienced a median recurrence-free survival of 13.4 months. This study demonstrates that personalized mRNA vaccines are feasible and capable of eliciting immune responses that may delay PDAC recurrence, paving the way for further clinical research.

In their 2022 study, M.M. Awad et.al.(19) conducted a Phase Ib clinical trial to assess the safety and effectiveness of the personalized neoantigen vaccine NEO-PV-01 in combination with chemotherapy (pemetrexed and carboplatin) and the anti-PD-1 therapy pembrolizumab as a first-line treatment for advanced non-squamous non-small cell lung cancer (NSCLC). The study included 38 patients, each of whom received a customized vaccine targeting up to 20 tumor-specific mutations (neoantigens) identified through genetic sequencing of their tumors. The treatment was well-tolerated and stimulated robust immune responses, including activation of neoantigen-specific CD4+ and CD8+ T cells. Some patients also exhibited epitope spreading, where their immune systems began targeting additional tumor mutations beyond those included in the vaccine. These findings suggest that combining NEO-PV-01 with standard therapies could provide a safe and effective approach to enhancing immune responses in patients with advanced NSCLC, warranting further research.

The study by Gal Cafri et.al. (20) investigated the safety and immunogenicity of a personalized mRNA vaccine in patients with metastatic gastrointestinal cancers. This Phase I/II clinical trial involved identifying tumor-specific mutations (neoantigens) from each patient's tumor and encoding them into an mRNA vaccine. Four patients received multiple doses of the vaccine, which was well-tolerated with no severe side effects. The vaccine successfully stimulated neoantigen-specific CD8+ and CD4+ T cell responses in three patients, including responses against KRAS G12D mutations. However, no tumor regression or clinical response was observed. The authors concluded that while the vaccine shows promise in inducing immune responses, further research is needed to evaluate its clinical efficacy, particularly in combination with other immunotherapies such as checkpoint inhibitors or T cell-based therapies.

The study Z. Ding et.al. (21) investigated the safety and effectiveness of a personalized dendritic cell (DC) vaccine for patients with advanced lung cancer. In this pilot study, 12 patients underwent genomic sequencing to identify 13 to 30 unique neoantigen peptides, which were used to prepare patient-specific vaccines. The vaccines were well-tolerated and successfully triggered immune responses against the targeted neoantigens in most patients. Clinically, 25% of patients experienced significant tumor shrinkage, and 75% achieved disease control, demonstrating that the vaccine could slow or stabilize tumor progression. The study concluded that this personalized immunotherapy approach shows promise as a safe and effective treatment for advanced lung cancer, warranting further research to enhance its efficacy.

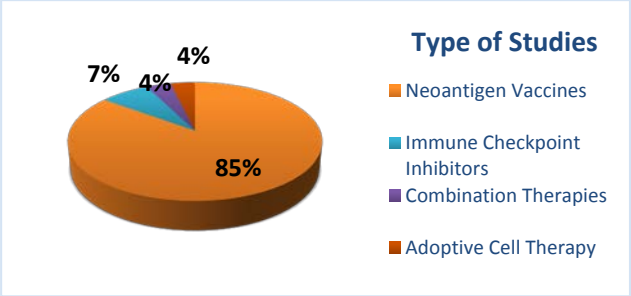

Figure 2. Distribution of Study Focus in Cancer Immunotherapy Research

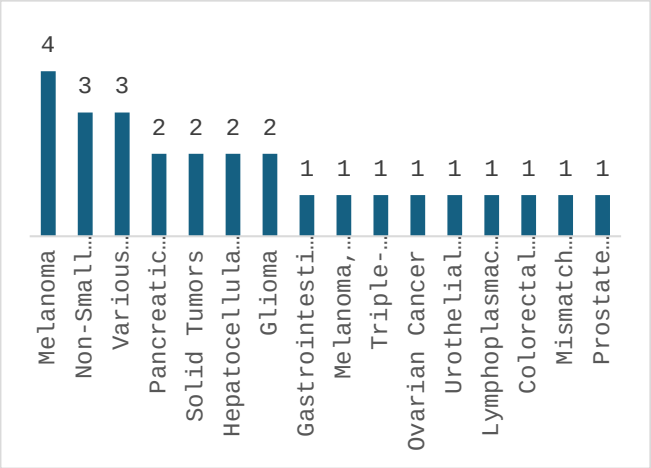

Figure 3. Immunotherapy Studies Across Various Cancers

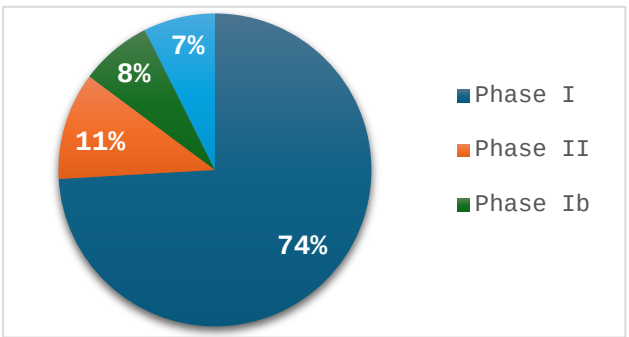

Figure 4. Immunotherapy Studies: Percentage of Trials by Phase.

The study by Ott et al. (2020) (22) explored the safety, feasibility, and effectiveness of combining a personalized neoantigen vaccine (NEO-PV-01) with the anti-PD-1 therapy nivolumab in patients with advanced melanoma, non-small cell lung cancer (NSCLC), or bladder cancer. This phase Ib trial included 82 participants and used a custom vaccine developed from each patient's tumor-specific mutations. The results showed that the combination was safe and well-tolerated, with no significant adverse effects. It successfully triggered strong immune responses, generating tumor-specific T cells capable of targeting and killing cancer cells. Additionally, the study observed "epitope spreading," where the immune response extended to other tumor antigens not included in the vaccine. These findings suggest that combining neoantigen vaccines with immune checkpoint inhibitors could be a promising strategy for treating advanced cancers.

The study by Palmer et al. (2022) (23) assessed the safety, tolerability, and immune response of a personalized neoantigen vaccine strategy for patients with advanced metastatic solid tumors. This phase 1/2 trial utilized a heterologous vaccine approach, starting with a chimpanzee adenovirus (ChAd68) prime dose followed by self-amplifying mRNA (samRNA) booster doses, both encoding up to 20 tumor-specific neoantigens. Patients also received immune checkpoint inhibitors, ipilimumab and nivolumab. The vaccine was generally well-tolerated, though some patients experienced mild to moderate side effects, with a few reporting serious adverse events. The vaccine generated T cell responses, particularly against TP53 neoantigens, suggesting differences in immune dominance between target antigens. Despite inducing immune responses, the treatment showed limited clinical benefit, with no tumor responses and modest survival outcomes. These findings are being used to refine the vaccine design, particularly to better target KRAS mutations, in ongoing trials.

The study by Yarchoan et al. (2024) (24) investigated the safety, immune effects, and efficacy of a personalized neoantigen vaccine combined with pembrolizumab in patients with advanced hepatocellular carcinoma (HCC) who had progressed on or could not tolerate first-line treatments. This phase 1/2 trial involved a DNA-based vaccine encoding up to 40 tumor-specific neoantigens, co-administered with an interleukin-12 plasmid, and pembrolizumab given every three weeks. The therapy was generally well-tolerated, with most side effects being mild injection-site reactions. Clinical responses were promising, with an objective response rate of 30.6%, including complete responses in 8.3% of patients. The vaccine induced robust T cell responses in most evaluable patients, with evidence of T cell expansion and tumor infiltration. These findings suggest that the vaccine, in combination with pembrolizumab, has potential as a treatment to enhance anti-tumor immunity in advanced HCC.

The study by Platten et al. (2021) (25) investigated the safety and immune response of a peptide vaccine targeting the IDH1 R132H mutation in patients with newly diagnosed gliomas. In this phase I trial, 33 patients received the IDH1-vac vaccine in addition to standard care, which included surgery, radiotherapy,

and chemotherapy. The vaccine was well-tolerated, with no significant adverse effects reported. A strong immune response against the IDH1 R132H mutation was observed in 93.3% of participants. Furthermore, patients who mounted an immune response to the vaccine experienced longer progression-free survival compared to those who did not. These results suggest that the vaccine is a safe and promising addition to standard treatments for gliomas with the IDH1 R132H mutation.

The study by Cai et al. (2021) (26) investigated the safety, feasibility, and potential effectiveness of personalized neoantigen vaccines in preventing postoperative recurrence in hepatocellular carcinoma (HCC) patients with vascular invasion. This single-arm trial included 10 patients at high risk of relapse after surgery, each receiving a vaccine customized to their tumor's unique mutations in a prime-boost schedule. The vaccine was well-tolerated, with no significant adverse effects. Among patients who completed the full vaccination course, robust neoantigen-specific T-cell responses were observed, correlating with longer recurrence-free survival. While 8 patients experienced relapse during follow-up, 2 remained recurrence-free, and personalized circulating tumor DNA (ctDNA) sequencing offered a real-time method for tracking disease progression and immune response. These findings suggest the vaccine's potential as a safe and personalized approach to reducing recurrence risk in HCC patients.

The study by Shou et al. (2022) (27) explored the potential of combining radiofrequency ablation (RFA) with personalized peptide neoantigen vaccines for cancer treatment. This study involved 28 cancer patients divided into two groups: one group received RFA within six months prior to vaccination, while the other did not. The vaccines were tailored to each patient's tumor-specific mutations and used GM-CSF as an adjuvant. Patients who received both RFA and the vaccine showed improved outcomes, with longer progression-free and overall survival compared to those who only received the vaccine. Enhanced neoantigen-specific T cell responses were also observed in this group. In preclinical mouse models, the combined treatment further suppressed tumor growth and extended survival compared to either treatment alone. These findings suggest that combining RFA with neoantigen vaccines could be a promising strategy for future cancer immunotherapy.

The study by Rappaport et al. (2024) (28) examined the safety, immune response, and feasibility of a shared neoantigen vaccine combined with immune checkpoint inhibitors in patients with advanced metastatic solid tumors. In this phase 1 trial, 19 patients received a vaccine targeting 20 shared neoantigens, including mutations in KRAS and TP53, delivered through a chimpanzee adenovirus vector (ChAd68) and self-amplifying mRNA (samRNA) boosters. This was paired with the immune checkpoint inhibitors ipilimumab and nivolumab. The treatment was generally well-tolerated, with mostly mild to moderate side effects, although two patients experienced severe adverse events. The vaccine-induced T cell responses, particularly against TP53 neoantigens, while responses to KRAS neoantigens were weaker. Despite immunogenicity, no clinical tumor responses were observed, with median progression-free and overall survival of 1.9 months and 7.9 months, respectively. These results emphasize the need to optimize vaccine designs, particularly to enhance responses against KRAS mutations, and ongoing phase 2 trials are addressing this.

The study by Zhang et al. (2024) (29) assessed the safety, feasibility, and effectiveness of personalized neoantigen DNA vaccines in patients with triple-negative breast cancer (TNBC) who had residual disease after chemotherapy and surgery. This phase 1 trial included 18 patients, each receiving a DNA vaccine encoding an average of 11 tumor-specific neoantigens administered intramuscularly in three doses. The vaccines were well-tolerated, with only mild side effects such as injection site reactions and flu-like symptoms. Immune responses specific to the targeted neoantigens were observed in 14 out of 18 patients. After a median follow-up of 36 months, 87.5% of patients remained recurrence-free, suggesting the vaccine may help prevent disease recurrence. These results highlight the vaccine's promise as a safe and effective adjuvant therapy for high-risk TNBC patients.

The study by Bobisse et al. (2023) (30) investigated the safety and potential benefits of combining a personalized dendritic cell vaccine with adoptive T cell therapy (ACT) in patients with advanced, treatment-resistant ovarian cancer. This phase 1 trial involved 19 patients, who first received an infusion of their own T cells, primed by a personalized vaccine, followed by repeated vaccine doses. The treatment was generally well-tolerated and showed encouraging outcomes, with 12 out of 17 patients achieving disease control within three months. The median overall survival was 14.2 months, significantly longer than the typical six months seen with standard fourth- or fifth-line chemotherapy. The therapy also reinvigorated anti-tumor immune responses, correlating with improved patient outcomes, highlighting the potential of this combination approach for advanced ovarian cancer.

A recent study by LA Rojas et.al. (18) explored the use of personalized mRNA vaccines targeting tumor-specific neoantigens in patients with pancreatic ductal adenocarcinoma (PDAC), a highly aggressive cancer with limited treatment options. In this phase 1 trial, patients with resected PDAC received individualized vaccines designed to stimulate immune responses against their unique tumor mutations. The vaccines were well-tolerated, with no major side effects reported. Approximately 50% of the patients exhibited strong T-cell responses to the neoantigens, and those who mounted these immune responses experienced longer recurrence-free survival. These findings suggest that personalized mRNA vaccines may offer a promising therapeutic strategy for PDAC and warrant further investigation.

The study by D'Alise et al. (2024) (31) investigated the safety and effectiveness of NOUS-PEV, a viral vector-based personalized vaccine, combined with pembrolizumab in patients with metastatic melanoma. This phase Ib trial included six patients who received vaccines designed to target up to 60 tumor-specific neoantigens identified from their individual tumor mutations. The vaccination regimen used a Great Ape Adenoviral vector (GAd20) for priming and Modified Vaccinia Ankara

(MVA) for boosting, alongside pembrolizumab, an anti-PD-1 therapy. The treatment was well-tolerated, with only mild vaccine-related side effects reported. All patients who completed the regimen developed robust neoantigen-specific T-cell responses, including CD4+ and CD8+ T cells targeting multiple antigens. Tumor biopsies from responding patients showed that vaccine-induced T cells effectively infiltrated tumors. These results highlight the potential of NOUS-PEV in combination with checkpoint inhibitors to enhance antitumor- immunity and support further exploration of this approach.

The review by Latifyan S. et al. (32) discusses recent advancements in personalized neoantigen vaccines for melanoma, summarizing findings from various clinical trials and studies. The authors highlight that these vaccines, tailored to the unique mutations in each patient's tumor, have shown promising results in activating robust anti-tumor immune responses. Clinical trials report prolonged progression-free survival and, in some cases, complete tumor regression. The vaccines are generally well-tolerated, with mild side effects like injection site reactions and flu-like symptoms. Strong T-cell responses specific to the targeted neoantigens indicate their effectiveness. The authors conclude that personalized neoantigen vaccines mark a significant step forward in melanoma treatment and emphasize the need for further research to optimize vaccine strategies and explore combination therapies for improved outcomes.

The study by Ingels et al. (2023) (33) investigated the safety and immune effects of dendritic cell (DC) vaccines targeting tumor-specific neoantigens in patients with advanced non-small cell lung cancer (NSCLC). In this phase I trial, neoantigens were identified from each patient’s tumor using sequencing and bioinformatics, and DCs were loaded with these neoantigens to create personalized vaccines. The vaccines were well-tolerated with no significant adverse events. T-cell responses specific to the neoantigens were observed in 7 of 10 patients, involving both CD4+ and CD8+ T cells spanning a range of differentiation states, from naïve to memory cells. Importantly, these immune responses were long-lasting, persisting for up to 12 months. The findings suggest that neoantigen-targeted DC vaccines are a safe and promising immunotherapy for NSCLC, warranting further research.

The study by Holm JS et al. (34) explored how neoantigen-specific CD8+ T cell responses in peripheral blood correlate with treatment outcomes in patients with metastatic urothelial carcinoma (mUC) undergoing PD-L1 blockade therapy. In this analysis of 24 patients from a clinical trial, researchers tracked neoantigen-reactive T cells (NARTs) before and three weeks after treatment using advanced peptide-MHC multimers. Patients who achieved disease control showed an increase in the diversity and number of NART populations, compared to those with disease progression. These T cells exhibited an effector phenotype marked by PD1+ Ki67+ and higher CD39 expression, distinguishing them from bystander or viral antigen-specific T cells. The findings suggest that the expansion of NARTs following PD-L1 blockade therapy could predict better outcomes, highlighting their potential as a biomarker for therapeutic success.

The CAPTURE study, conducted by Fendler A. et al., (35) examined immune responses to COVID-19 vaccination in cancer patients, focusing on adaptive immunity and neutralizing antibodies (NAb) against SARS-CoV-2 variants of concern (VOCs). The study included 585 patients with solid tumors or hematological malignancies who received two doses of either the Pfizer-BioNTech or AstraZeneca vaccine. Seroconversion rates were high in patients with solid tumors (85%) but lower in those with hematological cancers (59%). While most patients developed antibodies, their neutralizing antibody levels against VOCs, such as Alpha, Beta, and Delta, were lower than against the wild-type virus, especially in patients with hematological malignancies. Robust T cell responses were observed in 80% of patients across all cancer types, irrespective of the vaccine. Prior SARS-CoV-2 infection significantly boosted antibody responses, while anti-CD20 therapy was associated with undetectable antibody levels. The findings highlight that while T cell responses to vaccines remain strong, cancer patients, particularly those with blood cancers, may require tailored vaccination strategies to improve protection against VOCs.

The study by Podaza E. et al.(36) examined immune responses in cutaneous melanoma patients treated with the CSF-470 allogeneic cell-based vaccine combined with BCG and GM-CSF as part of the CASVAC-0401 Phase II trial. The study compared this vaccine regimen to intermediate-dose interferon-alpha 2b in patients with stage IIB, IIC, and III melanoma. The vaccine, made from irradiated cells from melanoma cell lines, elicited strong T-cell responses against shared melanoma-associated antigens and patient-specific predicted neoantigens, as shown by increased interferon-gamma activity in ELISPOT assays. Delayed-type hypersensitivity reactions correlated with stronger immune responses, and T-helper cell profiles suggested that certain immune markers might impact distant metastasis-free survival. In one case, vaccinated patient T cells demonstrated the ability to recognize and kill autologous tumor cells. These results highlight the CSF-470 vaccine's potential as an effective adjuvant therapy in melanoma, offering robust immune activation against both shared and unique tumor antigens.

The study by Szymura SJ et al. (37) investigated the safety and potential benefits of personalized neoantigen DNA vaccines as an early intervention for patients with untreated lymphoplasmacytic lymphoma (LPL), a slow-growing B-cell lymphoma. In this phase 1 non-randomized trial, nine asymptomatic patients received vaccines designed to target tumor-specific neoantigens identified through sequencing. The vaccines were well-tolerated, with no significant toxicities reported. Clinically, all patients experienced stable disease or better, with a median time to progression of over 72 months, and one patient showed a minor response. Immunogenicity analysis revealed a reduction in tumor B cells and their survival pathways, indicating an active immune response, though clonal plasma cells were unaffected. These findings suggest that personalized neoantigen vaccines are a safe and promising approach to delay disease progression in LPL and merit further exploration.

The study by Yu YJ et al. (38) examined the safety and effectiveness of personalized neoantigen vaccines in patients

with microsatellite-stable (MSS) advanced colorectal cancer (CRC), particularly those who had experienced recurrence or metastasis after surgery and chemotherapy. In this preliminary trial involving six patients, researchers identified specific neoantigens from tumor samples and created personalized vaccines targeting those antigens. The vaccines were well-tolerated with no serious side effects. Four out of six patients showed immune responses to the vaccines, and those who responded had significantly longer progression-free survival (PFS) compared to non-responders. Additionally, most patients experienced improvements in quality of life. The study suggests that personalized neoantigen vaccines are a promising and safe treatment option that could help extend survival in MSS-CRC patients.

The study by Engelhard VH et al. (39) explored the safety and effectiveness of a vaccine targeting MHC-restricted phosphopeptide antigens in patients with high-risk melanoma. In this phase I clinical trial, participants received a vaccine containing synthetic phosphopeptides derived from tumor-associated antigens, which were designed to stimulate CD8+ T cell responses. The vaccine was well-tolerated, with no serious side effects, and successfully induced strong T cell responses in the participants. Some patients showed stable disease or partial responses, indicating the potential for therapeutic benefit. These results suggest that this MHC-restricted phosphopeptide vaccine could be a promising treatment option for high-risk melanoma and warrants further investigation.

The study by Mueller S. et al. (40) explored the safety and effectiveness of a personalized vaccine targeting the H3.3K27M mutation in patients with diffuse midline glioma (DMG), including diffuse intrinsic pontine glioma (DIPG). In this phase I clinical trial, 19 patients with DIPG and 10 with nonpontine DMG received a peptide vaccine designed to target the H3.3K27M mutation, along with an immunostimulant, poly-ICLC. The vaccine was well-tolerated with no severe side effects, though injection site reactions were common. Mass cytometry analysis showed that patients who developed immune responses specifically targeting the H3.3K27M mutation had a significantly longer overall survival (16.1 months compared to 9.8 months). The study suggests that the H3.3K27M peptide vaccine could improve survival in these patients and warrants further investigation in larger trials.

The study by Poran A. et al. (41) explored how analyzing T-cell receptor (TCR) repertoires and blood cell phenotypes could predict melanoma patients' responses to personalized neoantigen therapy combined with anti-PD-1 treatment. In this research, 21 patients with metastatic melanoma were given a personalized vaccine targeting tumor neoantigens along with anti-PD-1 therapy. The researchers found that patients who showed positive responses to the treatment had a more diverse TCR repertoire and specific blood cell markers associated with strong immune activity. These findings suggest that profiling TCR repertoires and blood cell phenotypes could serve as useful tools to predict treatment success and help personalize immunotherapy strategies for melanoma patients.

The study by Kloor M. et al. (42) investigated the safety and immune response of a vaccine targeting frameshift peptide (FSP) neoantigens in patients with mismatch repair-deficient (dMMR) cancers, such as those associated with Lynch syndrome. In this phase I/IIa trial, patients received three cycles of subcutaneous vaccinations with FSPs derived from specific mutated genes, combined with an adjuvant to enhance immune responses. The vaccine was well-tolerated, with no serious side effects, and all patients developed T-cell responses specific to the FSPs, indicating strong immune activation. While some patients showed stable disease or partial responses, these results suggest that the vaccine has potential therapeutic benefits and warrants further development.

The study by Abdul Sater H. et al. (43) explored the impact of the neoadjuvant PROSTVAC vaccine on T-cell infiltration in the tumor microenvironment of men with localized prostate cancer. In this phase II trial, 27 patients received PROSTVAC prior to undergoing radical prostatectomy. The results showed a significant increase in both CD4 and CD8 T-cell infiltration in prostate tissue after vaccination, indicating enhanced immune activity within the tumor. Additionally, 52% of patients developed immune responses to non-neoantigens, suggesting systemic immune activation. The vaccine was well-tolerated with no serious side effects. These findings support further research into PROSTVAC as a potential immunotherapy for prostate cancer (44).

CONCLUSION

Neoantigen-based cancer vaccines represent a significant advancement in precision oncology, utilizing tumor-specific mutations to drive highly personalized and effective immune responses. Recent clinical trials have demonstrated their safety and feasibility, with promising outcomes in triggering strong immune activity and providing clinical benefits across diverse cancer types. However, several challenges remain. Tumor heterogeneity complicates the identification of consistent therapeutic targets, while variations in individual immune responses and mechanisms of tumor immune evasion can hinder the overall effectiveness of these vaccines. Progress in genomic sequencing and bioinformatics has been instrumental in advancing vaccine design, but further innovations are needed to refine their accuracy and enhance their impact. Combining neoantigen vaccines with complementary treatments, such as immune checkpoint inhibitors or adoptive T -cell therapies, offers potential solutions to these obstacles. As research continues, neoantigen-based vaccines are expected to revolutionize cancer therapy by providing safer, more targeted, and highly effective treatments tailored to each patient, redefining the possibilities of personalized medicine.

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Conflict of interest

No conflict of interest.

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