BIBLIOGRAPHIC INFORMATION SYSTEM

Journal Full Title: Journal of Biomedical Research & Environmental Sciences

Journal NLM Abbreviation: J Biomed Res Environ Sci

Journal Website Link: https://www.jelsciences.com

Journal ISSN: 2766-2276

Category: Multidisciplinary

Subject Areas: Medicine Group, Biology Group, General, Environmental Sciences

Topics Summation: 133

Issue Regularity: Monthly

Review Process: Double Blind

Time to Publication: 21 Days

Indexing catalog: IndexCopernicus ICV 2022: 88.03 | GoogleScholar | View more

Publication fee catalog: Visit here

DOI: 10.37871 (CrossRef)

Plagiarism detection software: iThenticate

Managing entity: USA

Language: English

Research work collecting capability: Worldwide

Organized by: SciRes Literature LLC

IndexCopernicus ICV 2022: 83.03

License: Open Access by Journal of Biomedical Research & Environmental Sciences is licensed under a Creative Commons Attribution 4.0 International License. Based on a work at SciRes Literature LLC.

Manuscript should be submitted in Word Document (.doc or .docx) through

Online Submission

form or can be mailed to support@jelsciences.com

Vision: Journal of Biomedical Research & Environmental Sciences main aim is to enhance the importance of science and technology to the scientific community and also to provide an equal opportunity to seek and share ideas to all our researchers and scientists without any barriers to develop their career and helping in their development of discovering the world.

JOURNAL OF BIOMEDICAL RESEARCH & ENVIRONMENTAL SCIENCES
ISSN: 2766-2276
SUBJECT AREA(S): VACCINES
DOI: 10.37871

MINI REVIEW

Advances in Personalized Medicine: Personalized Neoantigen Vaccines and Immune Checkpoint Inhibitor Combination Treatments

Priya Hays*

Documentation Specialists, LLC, San Mateo, CA, USA

Abstract

Background: Solid tumor malignancies are a cause of mortality in adults, with growing prevalence in young adults. Chemotherapies in combination with immune checkpoint inhibitors have been shown to induce responses in these tumors through T cell responses, however non-responders in the clinical setting have been observed.

Methods: PubMed searches were conducted with the keywords "Cancer vaccines", "Personalized vaccines," "tumor neoantigens" and "cancer immunotherapies."

Results: Personalized neoantigen vaccines constructed from primarily DNA, RNA and peptides have been shown to generate CD4+ and CD8+ T cell responses, resulting in delay in tumor growth and tumor regression. Created from tumor specific antigens, they are unique to each patient. Experiments detecting for T cell responses and preclinical models have provided evidence for the safety, feasibility and clinical efficacy of personalized neoantigen vaccines and immune checkpoint inhibitor combination treatments.

Conclusion: Future research can be directed to developing personalized neoantigen vaccines-ICI combination treatments for treatment of cancer and hematologic malignancies.

Introduction

Cancer is among the one of the highest causes of mortality worldwide and is showing increasing incidence in young adults. Since chemotherapy is associated with less than favorably safety profiles, considerable number of patients cannot tolerate it. Combination strategies with pembrolizumab have been administered, but however meet with drug resistance and non-responders. Precision oncology, or personalized cancer medicines, are in increasing clinical utilization and have led to improved clinical outcomes and less side effects in patients. Personalized cancer medicines comprise targeted therapies and cancer immunotherapies.

Personalized neoantigen vaccines are customized vaccines

***Corresponding author(s)**

Priya Hays, Hays Documentation Specialists, LLC, San Mateo, CA, USA

Email: priya@haysdocumentationspecialists.com

DOI: 10.37871/jbres2069

Submitted: 15 February 2025

Accepted: 27 February 2025

Published: 28 February 2025

Copyright: © 2025 Hays P. Distributed under Creative Commons CC-BY 4.0

OPEN ACCESS

Keywords

- Solid tumors
- Cancer immunotherapies
- Cancer vaccines
- Personalized Neoantigen vaccines
- Combination treatment

BIOLOGY GROUP

VACCINES

VOLUME: 6 ISSUE: 2 - FEBRUARY, 2025

Scan Me

How to cite this article: Hays P. Advances in Personalized Medicine: Personalized Neoantigen Vaccines and Immune Checkpoint Inhibitor Combination Treatments. J Biomed Res Environ Sci. 2025 Feb 28; 6(2): 172-179. doi: 10.37871/jbres2069, Article ID: JBRES2069, Available at: https://www.jelsciences.com/articles/jbres2069.pdf

manufactured to treat an individual patient in contrast to shared or public vaccines that are constructed through shared antigens. These vaccine types have distinct characteristics in that personalized neoantigens are tumor specific antigens, or TSAs, that are formed from non-synonomous mutations in tumors unique to each patients, while shared antigens vaccines are formed from tumor associated antigens or TAAs that are formed from mutations that are common among tumors such as KRAS and EGFR that can treat multiple patients with the same vaccine. It was in fact major advancements in genomics and bioinformatics from massively parallel sequencing and epitope prediction that in part led to the development of personalized neoantigen cancer vaccines, with development of neoantigens having sensitivity to immunotherapies and NGS to predict personalized neoantigen as well as algorithms that predict "naturally recognized tumor neoepitopes that are associated with immune responses." Shared neoantigens form the basis for off-the-shelf vaccine therapies that are manufactured [1].

TSAs are more attractive immunological targets since they are more immunogenic and lead to less central tolerance and since the target is not expressed on normal cells, they have less propensity for autoimmunity, and are identified through whole exome sequencing and whole genome sequencing. Cancer vaccines have shown considerable promise for cancers with some of the highest post-recurrence rates and harshest tumor immunosuppressive environments and lowest survival rates such as glioblastoma and pancreatic cancer [1].

The main types of personalized cancer neoantigens are DNA vaccines, RNA vaccines, peptide vaccines (the most common) and dendritic cell vaccines. According to one review, "tumor vaccines are designed to enhance antigen presentation, activate antigen-specific effector function, and induce memory T cell-mediated killing, thereby exerting their immunotherapeutic effects. Traditional cancer vaccines designed to Target Tumor-Associated Antigens (TAAs) have limited success due to poor tumor specificity" [2]. Vaccines increase the number of T cells that recognize MHC peptides that are induced by pathogens [3]. Personalized neoantigen cancer vaccines hold promise since they attack tumor cells while sparing normal cells and are highly effective given with the highly variable mutation rate of cancers and tumor heterogeneity, and show great potential especially when combined with immune checkpoint blockade [3].

There exists significant evidence that the immune system can recognize tumor neoantigens. According to observations from mouse models, it was found that antitumor T cells can recognize aberrant peptides from TSAs, while another study found that somatic mutations were found to be a source of TSAs recognized by T cells in human tumors [1]. Similarly, the Rosenberg group found that two neoantigens on melanoma cells in a patient with melanoma caused complete tumor regression after adoptive transfer of ex-vivo TILs. Additionally, cancerous cells acquire genetic alterations that lead to the presence of neoantigens, which are part of the cancer acquiring immune tolerance through the elimination (the elimination of precancerous lesions prior to being symptomatic), equilibrium (immune system finds the lesion and prevents it from being clinically detectable) and escape phases (cancer becomes clinically detectable since antigens are lost), involving immune cells, the TME and tumor metabolism. Neoantigen vaccines seek to overcome the immunosuppressive environment. A number of studies eliciting data have supported the principle that neoantigen immunotherapies target tumors with a modest number of neoantigens.

Another preclinical model study by Ott PA, et al. [4] that used a complicated predictive approach that showed interestingly that neoantigens can be subdivided into dominant and subdominant antigens. According to Yarchoan, et al. [1] "they confirmed that the peptides

They used bound to their predicted HLA class I molecules. Second, they immunized the three patients with advanced melanoma with seven selected peptides. This is unique in that no other study has used lymphocytes from vaccinated individuals." T cells emerged specific for one of the seven peptides before vaccination and three of the seven peptides after vaccination. T cells expanded after vaccination and undetectable neoantigens before vaccination had induced T cell responses, showing that vaccination can induce non-naturally occurring neoantigen-specific T cell responses, dividing them into dominant neoantigens that "spontaneously induce T cell responses" and subdominant neoantigens that do not naturally induce immune responses and require immunization. As of December 2022, a total of 199 trials reported in one analysis with phase I studies

being the most numerous and predominant study type.

As Wu DW, et al. [2] state Compared to traditional vaccines, neoantigen vaccines have severe advantages: (1) They can effectively stimulate, enhance, and diversify antitumor T cell responses, maximizing therapeutic specificity and overcoming immune tolerance; (2) its strong affinity with Major Histocompatibility Complex (MHC) molecules can prevent immune cells from attacking normal cells of patients and ensure the safety of treatment; and (3) they are highly feasible, generally safe, and easier to manufacture. Preliminary efficacy has been observed in both animal models and clinical studies, and tumor neoantigen vaccines have a potential synergistic effect in combination with ICIs. Tumor neoantigen vaccines are expected to bring tumor immunotherapy to a new height, prolong patient survival, and benefit more patients mainly attributed to the rapidly development of two technologies: neoantigen prediction tools, and vaccine delivery platform. The advent of immunogenomics approaches has facilitated the development of cancer vaccines based on tumor-specific neoantigens derived from somatic alterations (for example, point mutations, insertions or deletions, gene fusions) [2].

Categories of neoantigen vaccines

Peptide vaccines: Forming a category of vaccines formed by small chains of amino acids corresponding to neoantigens from specific tumors, these peptides trigger an immune response through the presentation of T cells to tumors, attacking and killing cancer cells. One example of a peptide vaccine is NeoVax which elicited a CR when PD-1 therapy was initiated following disease recurrence. The Neo-PV-01 entered into a phase 1b clinical trial in combination with pembrolizumab in 82 patients with advanced melanoma, non-small cell lung cancer, and bladder cancer, and demonstrated the presence of CD4+ and CD8+ T cell response subsequent to vaccination. These vaccines hold promise for eliciting highly targeted responses and as well as for their manufacturing process [4].

Another formulation of peptides vaccines are that they contain 8-12 amino acids derived from tumor antigens which also include MHC binding peptides that are endocytosed, processed and presented to professional APCs to lead to the production of "peptide-specific T cells." SLP, or synthetic long peptide, vaccines lead to more broader and diverse immune response that "enhance vaccine effectiveness by targeting a wider range of antigens or strains." Combined with other agents such as GM-CSF, polyriboinosinic-polyribocytidylic acid-poly L-Lysine Carboxymethylcellulose (poly-ICLC), Cytosine-Phosphateguanine (CPG) and Toll Like Receptor (TLR), T cell priming is optimized and antigen delivery efficiency. A phase I clinical trial for glioblastoma involved the delivery of a two vaccines, one derived from pre-manufactured unmutated antigens and one derived from neoantigens elicited sustained memory CD4 and CD8 T cells [5].

RNA vaccines: Using mRNA to construct a vaccine, RNA vaccines elicit T cell response to produce tumor specific neoantigens and trigger an immune response, and have been optimized by technological advancements that enhanced their stability, delivery methods and cost-effectiveness as well as their backbone structure. The two COVID-19 mRNA vaccines brought mRNA vaccines back into the spotlight. Being flexible and versatile, they lead to tumor antigens and other immunomodulatory molecules and inducing innate and adaptive immunity [6]. In 2017 the first clinical trial involving mRNA neoantigen vaccines took place and showed a robust and targeted T cell response in advanced melanoma and "vaccine-induced T cell infiltration and neoepitope-specific killing of autologous tumor cells." Known as the first personalized cancer vaccine, the mRNA vaccine mRNA-4157 was evaluated in a trial that comprised 13 patients in a monotherapy group and after a median follow-up of 8 months, 12 patients remained disease-free. Additionally, 20 patients received combination therapy 1 achieved CR, 2 had partial stable disease, 5 had disease progression, 2 had unconfirmed disease progression, supporting advancement to phase 2. Based on data from the phase IIb KEYNOTE-942, the combination of mRNA-4157/V940 vaccine with pembrolizumab led to a 44% reduction in disease recurrence in 157 patients with surgically resectable high-risk melanoma, with mild adverse effects reported, leading to FDA approval in combination with anti-PD-1 therapy in advanced melanoma patients in the adjuvant setting. A lipid nanoparticle coated neoantigen mRNA vaccine with driver gene mutations tandemly linked into a single mRNA sequenced administered to patients with GI cancer. Neoantigens and "driver gene mutations were tandemly linked into a single mRNA sequence, coated with LNP, and administered to patients with

gastrointestinal cancer," elicited a robust and broad immune response. In a randomized phase 2 trial, the individualized mRNA neoantigen cancer vaccine BNT122 in combination with pembrolizumab was utilized to treat advanced melanoma, and induced a response in surgically resectable pancreatic cancer tumors which also led to a robust and specific T cell response and recurrence free survival [4]. Due to their lower risk for mutagenesis and autoimmune and absence of HLA restriction they lead to the capability of targeting multiple neoantigens along with their ease and rapidity, neoantigen RNA vaccines "hold great potential for cancer immunotherapy" [3].

DNA vaccines: DNA vaccines are formed by the DNA fragments that encode specific neoantigens that are translated into proteins presented to the immune system leading to an immune response and the elimination of tumor cells that express the targeted neoantigen. Their advantage lies in producing a vector that expresses both tumor antigen and adjuvant, with plasmid and viral based being the two types. Plasmid based DNA vaccines are designed through directly injectable DNA that are delivered through electroporation as one method while viral based DNA vaccines use a virus that is genetically modified to deliver the DNA. One DNA vaccine in a phase 2/3 study GRT-C901/GRT-R902 is being combined with ICB for mCRC patients administered through intramuscular injection. However they are limited by being weak and having a short-lived response along with physical barriers [5].

There are a number of DNA vaccines undergoing studies, one being GX-188E against HPV-16/HPV-18 administered to patients diagnosed with cervical cancer positive for HPV virus. Remission was achieved in 19 of 60 patients [ORR 31.7%] with CR being 6/60 and PR being 13/60. The vaccine along showing clinical efficacy, the safety profile was excellent. Another plasmid DNA vaccine was constructed through encoding HER2/neu which also led to an antigen-specific T cell response with persistence after vaccine. [Fan] DNA vaccines can also administer other immunostimulatory cytokines such as GM-CSF and IL-2 [5].

Cell based vaccines: Cell based vaccines take the form of dendritic cell vaccines that take a patient's DC and load the DC's with neoantigens (peptides (most utilized), mRNA or DNA) and have emerged as a promising approach due to high immunogenicity, specificity and safety and long-lasting immunity. After injection or intravenous administration, they stimulate a specific T cell response leading to tumor killing. According to Li, "[p]eptide-pulsed DC vaccines have demonstrated an augmented spectrum and diversity of neoantigen-specific T cells in melanomas and advanced lung cancer." Neo-DCVac, a peptide DC vaccine, was evaluated in a phase I trial and had robust clinical activity in 12 lung cancer patients, with a DCR of 75% and mPFS of 5.5 months and mOS of 7.9 months. Neo-MoDC vaccine was combined with ICI therapy and evaluated in a phase I trial for metastatic GC and was also shown to have similar promise. However these vaccines are limited due to complexity and cost of preparation. DCVax-L an autologous tumor lysate-loaded DC vaccine was shown in a phase 3 trial to treat newly diagnosed glioblastoma and recurrent glioblastoma, with nGBM patients having a median OS of 19.3 months, longer than the 16.5 months in control groups. (HR = 0.80; 98% CI, 0.00-0.94; p = 0.002). rGBM patients had a median OS of 13.2 months compared to 7.8 months on those without treatment [3,5].

64.8% of all clinical trials involved peptide vaccine and delivery platforms, with 16.1% for the DC system, and 5.5% for LNP. Most vaccines were applied as monotherapy with some combination therapies with immunotherapies evaluated. Tumor types involved including unspecified solid tumors (25.1), NSCLC (12.1%) and pancreatic cancer (7.5%) [4].

ICI and personalized neoantigen vaccines combination therapies

Termed an "immunotherapy duo", the combination of immune checkpoint inhibitors and personalized neoantigen cancer vaccines have been shown to sustain the anti-tumor immune response of vaccines and that there are preclinical and clinical studies with data supporting the synergy of anti-PD-1 ICIs with neoantigen vaccines [2].

An early neoantigen vaccine and immune checkpoint inhibitor combinations reported was a peptide generated vaccine, and demonstrated the feasibility, safety and tolerability of a NEO-PV-01 in a phase1b single arm study in combination with chemotherapy and pembrolizumab as first-line therapy in non-squamous NSCLC. PD-L1 status determined patient enrollment with primary endpoint being safety and secondary endpoints being PFS, OS and ORR. Combination vaccine treatment was observed to lead to cytotoxic T cell infiltrate and was

shown to be immunogenic. The vaccine was composed of peptides, specifically, poly-ICLC (polyinosinic-polycytidylic acid stabilized with polylysine and carboxymethylcellulose.

Dosing instructions included patients receiving the combination treatment every 3 weeks in 4 cycles with five priming and two booster doses of NEO-PV-01, continued until either toxicities developed or disease progression.

Mutational status observed in NSCLC among an ITT set of 38 patients

Mutation	# of patients
KRAS mutation	19
TP53	15
KEAP1	6
STK11	No mutations

Key Results

- "Median PFS (95% CI) for ITT patients was 6.3 months (5.6–14.7) and for VAX patients was 7.2 months (5.7–14.7).
- Median OS for ITT patients was 16.8 months and for VAX patients was 20 months (11.6, NR ITT set, 11.5, NR VAX group)."

MHC Class II expression was observed in a monocytic lineage with tumor infiltration of CD4+ T cells and CD8+ T cells in the outside of tumor areas. Immune response was proportional to the presence of vaccine peptides and was observed in 13 patients when assessed 8 weeks after the first dose. Ex vivo responses were observed in all patients (100%), with a 94% response rate post-vaccination. 19 patients with KRAS mutations were observed to have immune responses, suggesting its immunogenicity is driving clinical outcomes. The authors concluded that safety, feasibility, and clinical efficacy were observed in patients receiving NEO-PV-01 vaccine in combination treatment and also suggested that oncogenic mutations such as KRAS may be driving response with epitope spread also observed [6,7].

Lin MJ, et al. [8] evaluated the regimen of bevacizumab, an anti-angiogenic agent, with a DNA viral vaccine that leads to T-cells entering tumor cells in non-small cell lung cancer. LLCVac, 7 novel immunogenic peptides, were also created that elicited a strong immune response, leading to decreases in tumor volume with a favorable adverse event profile. With the Ki67 tumor marker being found, the study remains highly significant finding since NSCLC is resistant to immune checkpoint inhibitors and chemotherapy. Tumor efficacy was determined by evaluation of in vivo tumor models. Mice were divided into four experimental groups after being injected subcutaneously with tumor cells. When tumor volume gera 50–80 mm3 on day 0, they were injected with LLCvac the neoantigen peptide vaccines (100 peptides/mouse) with dual immune adjuvants and compared saline controls. Bevacizumab (Bev: 5 mg/kg, 100 µg/mouse, Roche Diagnostics GmbH, Germany) was injected into mice with growing tumors and anti-PD-1 antibody (2.5 mg/kg, 50 µg/mouse, Leinco Technologies, USA) or the combination of LLCvac and anti-PD-1 + Bev twice weekly for 2 weeks. Single cell sequencing determined T cell infiltration. Whole transcriptome and whole exome sequencing of LLC cells and C57BL/6 mice to identify tumor antigen mutations. 762 mutations were identified and RNA analysis showed a variant allele frequency ≥ 10%, read depth ≥ 20 and transcripts per million of the corresponding gene ≥ 1. 7 out of 16 long peptides showed immunogenicity. The growth rate of the tumor was shown to be slowed down and induced potent anti-tumor response since the "maturity of lymph node DC (CD80+ and CD86+) and the amount of spleen immune memory T cells (CD44+ and CD62L-) were significantly increased in the LLCvac group, indicating the neoantigen vaccine was successful in targeting the tumor and led to systemic immune response. Immunofluorescence staining of CD4+ and CD8+ T cells showed activity of T cells in the tumor microenvironment. (p = 0.0196 and p = 0.0071). Further investigated was whether the bevacizumab would augment the shrinkage of the tumor volume and lead to slowing of tumor growth rate, and it was determined experimentally that the efficacy of Bev and anti-PD-1 was better than the monotherapy groups, and is consistent with clinical performance. Significantly it was also found that Mki67 a marker of active cell proliferation was expressed under stimulation of tumor antigens in vaccines, suggestive of better prognosis in solid tumors. Differentiation of naïve T cells into Mki67 differentiated T cells was found to be induced by the combined therapy [9-11].

The combination of pembrolizumab and a neoantigen DNA plasmic vaccine, PCTV, composed of 40 neoantigens, co-administered with IL-12, to patients with hepatocellular carcinoma, which showed improvement over PD-1 monotherapy. Safety

and immunogenicity were primary endpoints and efficacy and feasibility were secondary endpoints. According to RECIST criteria, "30.6% (11 of 36 patients), with 8.3% (3 of 36) of patients" achieved a complete response. T cell responses to the neoantigens were confirmed in 86.4% or 19/22 patients. Bulk sequencing revealed T cell expansion and infiltration as a result of vaccination. 75 patients were observed to have low grade TRAEs and with no grade ≥3 TRAEs 8.3% of patients showed an irAE that required systemic corticosteroids including "grade 2 nephritis, grade 2 pneumonitis and grade 2 hepatitis)." "One patient (2.8%) discontinued pembrolizumab owing to an adverse event, but no patients discontinued PTCV therapy because of an adverse event." ORR was 30.6% with 8.3% achieving a complete response (3 of 36) and 22.2% (8 of 36) achieving a partial response. DCR was 55.6% (20 of 36 patients). mPFS was 4.2 months and mOS was 19.9 months. ctDNA baseline analysis was conducted showing a molecular response as 50% reduction in ctDNA levels. These results were observed in patients receiving 40 neoantigens. T cell biomarkers CD8A, CD8B, CCL5, CXCR6, LCK and TIGIT were increased in responders versus non-responders. mOS as distinguished by IFN-gamma response showed was 30.2 versus 15.7 months. Pembrolizumab in combination with PCTV induced responses in hepatocellular carcinoma, quite possibly eliminating hepatotoxicity induced symptoms.

An M38 tumor model was developed by Salvatori E, et al. [12] that was tested in combination with anti-CTLA-4 inhibitors to generate T cell responses in colon cancer. C20 a vaccine expressing 20 C26 neoantigens also generated CD4+ and CD8+ T cells in vivo and led to tumor delay. IL17A cytokine release was detected in the inflammatory response and relieved. Tumor regression was also seen in cotreated animals, with tumor stabilization seen in the monotherapy group. T cell depletion experiments showed that the mechanism of action was the anti-tumor activity induced by the cotreatment of immune checkpoint inhibitor and neoantigen vaccine.

Discussion

Personalized cancer vaccines can induce anti-tumor response and lead to tumor regression in combination with immune checkpoint inhibitors in solid tumors such as NSCLC and melanoma. Malignancies such as glioblastoma and ovarian cancer are also under investigation for this co-treatment combination, also termed the immunotherapy duo and cancer vaccines are have been termed the new frontier in immunotherapies [13], also suggesting that this intervention could be combined with radiotherapy. Huang reported that in poorly immunogenic tumors such as colorectal cancer and triple negative breast cancer that cancer vaccines would lead to antitumor immunity [14]. Tanyi JL, et al. [15] reported similar results for ovarian cancer demonstrating the eliciting of a polyfunctional T cell response. Circumventing immunological tolerance and immunosuppression, cancer vaccines elicit local and systemic immune responses that are augmented by immune checkpoint inhibitors, as these reviews and studies have provided evidence for Safety considerations are addressed significantly in the evaluation of the mRNA COVID-19 vaccines in the literature. One review stated key results for the clinical vaccine efficacy of the BNT162b2 vaccine in data from a study in the UK. A 90% efficacy upon initial dosing that dropped to 60% after 25 weeks was shown. The efficacy of ChAdOx1 nCoV19 dropped to 40% as well, due to waning immunity and decrease in virus specific antibodies [16]. Third doses of the mRNA vaccine were shown to mitigate against this waning immunity and protect against emerging variants. A study conducted between 2021 and 2022 evaluating vaccine efficacy in series demonstrated comparative effectiveness of the third dose of BNT162b2 or mRNA-1273 vaccines in approximately in eligible 65,000 US veterans who received prior doses [17]. The number of infectious events decreased considerably after the third dose of BNT162b2 when compared with mRNA-1273:

- 45.4 (95% CI: 19.4, 84.7) (documented infection)
- 3.7 (2.2, 14.1) (symptomatic COVID-19)
- 10.6 (5.1, 19.7) (COVID-19 hospitalization)
- 2.0 (-3.1, 6.3) (COVID-19 intensive care unit admission)
- 0.2 (-2.2, 4.0) (COVID-19 death)

Copland E, et al. [18] performed an analysis on safety outcomes for 5.1 million children in UK who received the BNT162b2 vaccine. A favorable safety profile was reported with low rates of hospitalizations and adverse events. Cases of myocarditis were observed in 12-17 year olds (estimated 3 (95%CI 0-5) and 5 (95%CI 3-6) per million following a first and second dose with BNT162b2, respectively) and12 (95% 0-23) hospitalizations for epilepsy following

vaccination. SARS-CoV-2 infection was associated with increased risk of hospitalization due to systemic inflammation and myocarditis shown to be mitigated by vaccination.

Conclusion

Personalized cancer vaccines have been shown in preclinical models and phase 1 trials to treat solid tumor and augment clinical efficacy of immune checkpoint inhibitors in patients that do not respond to monotherapy chemotherapy combinations. Future research can be directed to understanding mechanisms behind delay in tumor growth and tumor regression.

Acknowledgment

P.H. wishes to thank the Editorial Team at JBRES for their flexibility.

References

1. Yarchoan M, Johnson BA 3rd, Lutz ER, Laheru DA, Jaffee EM. Targeting neoantigens to augment antitumour immunity. Nat Rev Cancer. 2017 Apr;17(4):209-222. doi: 10.1038/nrc.2016.154. Epub 2017 Feb 24. Erratum in: Nat Rev Cancer. 2017 Aug 24;17(9):569. doi: 10.1038/nrc.2017.74. PMID: 28233802; PMCID: PMC5575801.

2. Wu DW, Jia SP, Xing SJ, Ma HL, Wang X, Tang QY, Li ZW, Wu Q, Bai M, Zhang XY, Fu XF, Jia MM, Tang Y, Chen L, Li N. Personalized neoantigen cancer vaccines: current progression, challenges and a bright future. Clin Exp Med. 2024 Sep 26;24(1):229. doi: 10.1007/s10238-024-01436-7. PMID: 39325256; PMCID: PMC11427492.

3. Shavkunov AS, Gubin MM. The dynamics of an immunotherapy duo. Nat Cancer. 2022 Apr;3(4):376-378. doi: 10.1038/s43018-022-00362-5. PMID: 35484417.

4. Ott PA, Hu-Lieskovan S, Chmielowski B, Govindan R, Naing A, Bhardwaj N, Margolin K, Awad MM, Hellmann MD, Lin JJ, Friedlander T, Bushway ME, Balogh KN, Sciuto TE, Kohler V, Turnbull SJ, Besada R, Curran RR, Trapp B, Scherer J, Poran A, Harjanto D, Barthelme D, Ting YS, Dong JZ, Ware Y, Huang Y, Huang Z, Wanamaker A, Cleary LD, Moles MA, Manson K, Greshock J, Khondker ZS, Fritsch E, Rooney MS, DeMario M, Gaynor RB, Srinivasan L. A Phase Ib Trial of Personalized Neoantigen Therapy Plus Anti-PD-1 in Patients with Advanced Melanoma, Non-small Cell Lung Cancer, or Bladder Cancer. Cell. 2020 Oct 15;183(2):347-362.e24. doi: 10.1016/j.cell.2020.08.053. PMID: 33064988.

5. Keskin DB, Anandappa AJ, Sun J, Tirosh I, Mathewson ND, Li S, Oliveira G, Giobbie-Hurder A, Felt K, Gjini E, Shukla SA, Hu Z, Li L, Le PM, Allesøe RL, Richman AR, Kowalczyk MS, Abdelrahman S, Geduldig JE, Charbonneau S, Pelton K, Iorgulescu JB, Elagina L, Zhang W, Olive O, McCluskey C, Olsen LR, Stevens J, Lane WJ, Salazar AM, Daley H, Wen PY, Chiocca EA, Harden M, Lennon NJ, Gabriel S, Getz G, Lander ES, Regev A, Ritz J, Neuberg D, Rodig SJ, Ligon KL, Suvà ML, Wucherpfennig KW, Hacohen N, Fritsch EF, Livak KJ, Ott PA, Wu CJ, Reardon DA. Neoantigen vaccine generates intratumoral T cell responses in phase Ib glioblastoma trial. Nature. 2019 Jan;565(7738):234-239. doi: 10.1038/s41586-018-0792-9. Epub 2018 Dec 19. PMID: 30568305; PMCID: PMC6546179.

6. Fan T, Zhang M, Yang J, Zhu Z, Cao W, Dong C. Therapeutic cancer vaccines: advancements, challenges, and prospects. Signal Transduct Target Ther. 2023 Dec 13;8(1):450. doi: 10.1038/s41392-023-01674-3. PMID: 38086815; PMCID: PMC10716479.

7. Rojas LA, Sethna Z, Soares KC, Olcese C, Pang N, Patterson E, Lihm J, Ceglia N, Guasp P, Chu A, Yu R, Chandra AK, Waters T, Ruan J, Amisaki M, Zebboudj A, Odgerel Z, Payne G, Derhovanessian E, Müller F, Rhee I, Yadav M, Dobrin A, Sadelain M, Łuksza M, Cohen N, Tang L, Basturk O, Gönen M, Katz S, Do RK, Epstein AS, Momtaz P, Park W, Sugarman R, Varghese AM, Won E, Desai A, Wei AC, D'Angelica MI, Kingham TP, Mellman I, Merghoub T, Wolchok JD, Sahin U, Türeci Ö, Greenbaum BD, Jarnagin WR, Drebin J, O'Reilly EM, Balachandran VP. Personalized RNA neoantigen vaccines stimulate T cells in pancreatic cancer. Nature. 2023 Jun;618(7963):144-150. doi: 10.1038/s41586-023-06063-y. Epub 2023 May 10. PMID: 37165196; PMCID: PMC10171177.

8. Lin MJ, Svensson-Arvelund J, Lubitz GS, Marabelle A, Melero I, Brown BD, Brody JD. Cancer vaccines: the next immunotherapy frontier. Nat Cancer. 2022 Aug;3(8):911-926. doi: 10.1038/s43018-022-00418-6. Epub 2022 Aug 23. PMID: 35999309.

9. Awad MM, Govindan R, Balogh KN, Spigel DR, Garon EB, Bushway ME, Poran A, Sheen JH, Kohler V, Esaulova E, Srouji J, Ramesh S, Vyasamneni R, Karki B, Sciuto TE, Sethi H, Dong JZ, Moles MA, Manson K, Rooney MS, Khondker ZS, DeMario M, Gaynor RB, Srinivasan L. Personalized neoantigen vaccine NEO-PV-01 with chemotherapy and anti-PD-1 as first-line treatment for non-squamous non-small cell lung cancer. Cancer Cell. 2022 Sep 12;40(9):1010-1026.e11. doi: 10.1016/j.ccell.2022.08.003. Epub 2022 Aug 25. PMID: 36027916.

10. Lin X, Tang S, Guo Y, Tang R, Li Z, Pan X, Chen G, Qiu L, Dong X, Zhang L, Liu X, Cai Z, Xie B. Personalized neoantigen vaccine enhances the therapeutic efficacy of bevacizumab and anti-PD-1 antibody in advanced non-small cell lung cancer. Cancer Immunol Immunother. 2024 Jan 27;73(2):26. doi: 10.1007/s00262-023-03598-x. PMID: 38280084; PMCID: PMC10821847.

11. Yarchoan M, Gane EJ, Marron TU, Perales-Linares R, Yan J, Cooch N, Shu DH, Fertig EJ, Kagohara LT, Bartha G, Northcott J, Lyle J, Rochestie S, Peters J, Connor JT, Jaffee EM, Csiki I, Weiner DB, Perales-Puchalt A, Sardesai NY. Personalized neoantigen vaccine and pembrolizumab in advanced hepatocellular carcinoma: a phase 1/2 trial. Nat Med. 2024 Apr;30(4):1044-1053. doi: 10.1038/s41591-024-02894-y. Epub 2024 Apr 7. PMID: 38584166; PMCID: PMC11031401.

12. Salvatori E, Lione L, Compagnone M, Pinto E, Conforti A, Ciliberto G, Aurisicchio L, Palombo F. Neoantigen cancer vaccine augments anti-CTLA-4 efficacy. NPJ Vaccines. 2022 Feb 2;7(1):15. doi: 10.1038/s41541-022-00433-9. PMID: 35110563; PMCID: PMC8810847.

13. Lin MJ, Svensson-Arvelund J, Lubitz GS, Marabelle A, Melero I, Brown BD, Brody JD. Cancer vaccines: the next immunotherapy frontier. Nat Cancer. 2022 Aug;3(8):911-926. doi: 10.1038/s43018-022-00418-6. Epub 2022 Aug 23. PMID: 35999309.

14. Huang KC, Chen WT, Chen JY, Lee CY, Wu CH, Lai CY, Yang PC, Liang JA, Shiau AC, Chao KSC, Ke TW. Neoantigen-augmented iPSC cancer vaccine combined with radiotherapy promotes antitumor immunity in poorly immunogenic cancers. NPJ Vaccines. 2024 May 31;9(1):95. doi: 10.1038/s41541-024-00881-5. PMID: 38821980; PMCID: PMC11143272.

15. Tanyi JL, Chiang CL, Chiffelle J, Thierry AC, Baumgartener P, Huber F, Goepfert C, Tarussio D, Tissot S, Torigian DA, Nisenbaum HL, Stevenson BJ, Guiren HF, Ahmed R, Huguenin-Bergenat AL, Zsiros E, Bassani-Sternberg M, Mick R, Powell DJ Jr, Coukos G, Harari A, Kandalaft LE. Personalized cancer vaccine strategy elicits polyfunctional T cells and demonstrates clinical benefits in ovarian cancer. NPJ Vaccines. 2021 Mar 15;6(1):36. doi: 10.1038/s41541-021-00297-5. Erratum in: NPJ Vaccines. 2021 May 4;6(1):68. doi: 10.1038/s41541-021-00332-5. PMID: 33723260; PMCID: PMC7960755.

16. Fendler A, de Vries EGE, GeurtsvanKessel CH, Haanen JB, Wörmann B, Turajlic S, von Lilienfeld-Toal M. COVID-19 vaccines in patients with cancer: immunogenicity, efficacy and safety. Nat Rev Clin Oncol. 2022 Jun;19(6):385-401. doi: 10.1038/s41571-022-00610-8. Epub 2022 Mar 11. PMID: 35277694; PMCID: PMC8916486.

17. Dickerman BA, Gerlovin H, Madenci AL, Figueroa Muñiz MJ, Wise JK, Adhikari N, Ferolito BR, Kurgansky KE, Gagnon DR, Cho K, Casas JP, Hernán MA. Comparative effectiveness of third doses of mRNA-based COVID-19 vaccines in US veterans. Nat Microbiol. 2023 Jan;8(1):55-63. doi: 10.1038/s41564-022-01272-z. Epub 2023 Jan 2. PMID: 36593297; PMCID: PMC9949349.

18. Copland E, Patone M, Saatci D, Handunnetthi L, Hirst J, Hunt DPJ, Mills NL, Moss P, Sheikh A, Coupland CAC, Harnden A, Robertson C, Hippisley-Cox J. Safety outcomes following COVID-19 vaccination and infection in 5.1 million children in England. Nat Commun. 2024 May 27;15(1):3822. doi: 10.1038/s41467-024-47745-z. Erratum in: Nat Commun. 2024 Jul 8;15(1):5723. doi: 10.1038/s41467-024-50151-0. PMID: 38802362; PMCID: PMC11130197.

How to cite this article: Hays P. Advances in Personalized Medicine: Personalized Neoantigen Vaccines and Immune Checkpoint Inhibitor Combination Treatments. J Biomed Res Environ Sci. 2025 Feb 28; 6(2): 172-179. doi: 10.37871/jbres2069, Article ID: JBRES2069, Available at: https://www.jelsciences.com/articles/jbres2069.pdf