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Dendritic Cell-Based Vaccines in Cancer Therapy: Focus on Melanoma, Glioblastoma, and Prostate Cancers

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Abstract

Context:*Despite advances* in conventional cancer therapies, tumor recurrence and treatment-related toxicities remain major challenges. Dendritic cell (DC)-based vaccines have emerged as a promising immunotherapeutic approach, capable of activating tumor-specific T-cell responses across multiple malignancies, including melanoma, prostate cancer, and glioblastoma. This narrative review summarizes current evidence on dendritic cell-based immunotherapy, with a focus on clinical trials in prostate cancer, melanoma, and glioblastoma. It aims to evaluate the therapeutic potential of dendritic cell vaccines and their role in personalized and combination treatment strategies designed to overcome tumor heterogeneity and immune evasion.

Evidence Acquisition: A narrative literature search was conducted in PubMed for English-language human studies published between 2000 and 2026. Search terms included "glioblastoma", "melanoma", "prostate cancer", "dendritic cells", "cancer vaccines", "immunotherapy", "Sipuleucel-T", and "BPX-101". Boolean operators (AND/OR) were used to combine the search terms. Duplicate articles and unrelated studies were excluded after review of titles and abstracts.

Results: DC-based vaccines were generally safe and induced tumor-specific immune responses in melanoma, glioblastoma, and prostate cancer, although clinical outcomes were heterogeneous. In melanoma, immune activation was frequent, but the clinical benefit was limited. In glioblastoma, DCVax-L improved overall survival, whereas other approaches demonstrated immune responses without a clear survival benefit. In prostate cancer, Sipuleucel-T provided a modest survival benefit, whereas the phase III VIABLE trial (DCVAC/PCa) failed to improve overall survival. Engineered and biomaterial-based vaccine platforms showed immunogenicity but inconsistent clinical efficacy.

Conclusions: Overall, dendritic cell-based vaccines, despite eliciting antitumor immune responses, have not demonstrated meaningful improvements in survival outcomes (except for Sipuleucel-T). Therefore, optimization of therapeutic strategies and the use of combination approaches appear necessary to achieve clinically significant benefits.

Keywords: Dendritic Cell-based Vaccines, Cancer Immunotherapy, Melanoma, Glioblastoma, Prostate Cancer

1. Context

Cancer is defined as the uncontrolled proliferation of transformed cells (1) and constitutes a global burden, causing nearly 20 million new cases annually and projected to reach 35 million by 2050 (2). In Iran, it is the second-leading cause of death and is expected to surge by 67% by 2035. *Despite* substantial advancements in surgical techniques, radiotherapy, and cytotoxic chemotherapy, the clinical management of malignancy remains fraught with challenges, most notably the high propensity for tumor recurrence and the debilitating nature of treatment-induced toxicities. The persistence of minimal residual disease (MRD) following curative-intent interventions, coupled with the systemic and tissue-specific adverse effects inherent in conventional therapies, underscores the pressing need for

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therapeutic modalities that offer enhanced precision and durability (3-5).

Immunotherapy is an emerging field in cancer management in which new approaches are continuously being developed to improve patient outcomes. Moreover, immunotherapy aims to address limitations associated with conventional treatment modalities (6, 7). Cancer vaccines are one form of active immunotherapy and use specific formulations designed to elicit immune responses against tumors by targeting tumor-associated antigens (TAAs). Dendritic cell-based vaccines (DC-based vaccines) represent another promising approach because they can process and present multiple antigens, thereby promoting T-cell-mediated immunity (8). Studies of DC-based vaccines indicate that they effectively activate T cells capable of recognizing and eliminating cancers, with an acceptable safety profile. Since their laboratory discovery by Steinman and subsequent evaluation in clinical trials beginning in the 1990s, DC-based vaccines have been shown to induce activated immune cells within tumors and even in lesions outside the primary tumor (9).

Melanoma, glioblastoma (GBM), and prostate cancer were selected for this study because they represent cancers with distinct clinical and immunological profiles. Melanoma is widely recognized as one of the most immunogenic malignancies and has therefore served as a key model for evaluating the effectiveness of DC-based vaccines (10). In contrast, prostate cancer holds a unique position in the clinical development of DC vaccine strategies, largely due to the successful development and regulatory approval of Sipuleucel-T, the first FDA-approved DC-based therapeutic vaccine (11). GBM, on the other hand, presents a particularly challenging target because of its highly aggressive behavior and profoundly immunosuppressive tumor microenvironment (TME). Nevertheless, growing evidence from recent studies suggests that DC vaccines may offer therapeutic benefit in glioblastoma, with several trials reporting encouraging outcomes (12). Collectively, these three malignancies differ in immunological and clinical context and provide a comprehensive framework for evaluating the therapeutic potential, challenges, and future directions of DC-based cancer vaccines.

Despite advances in cancer immunotherapy, it remains essential to identify markers of effective antitumor immune responses, establish personalized therapy protocols, improve preclinical models for prediction, and combine therapies to maximize clinical outcomes (7). Further research into the properties of DCs may help address these needs and enhance the efficacy of immune stimulation directed against specific tumors. Thus, the present review aims to discuss the biology, modes of action, and clinical use of DC-based vaccines, as well as their advantages and the limitations of existing cancer immunotherapies.

2. Evidence Acquisition

A narrative literature search was conducted in PubMed for English-language human studies published between 2000 and 2026. Search terms included "glioblastoma", "melanoma", "prostate cancer", "dendritic cells", "cancer vaccines", "immunotherapy", "Sipuleucel-T", and "BPX-101". Boolean operators (AND/OR) were used to combine the search terms. Duplicate records and unrelated studies were excluded after review of the titles and abstracts.

3. Results

3.1. History, Fundamental Concepts, and Functional Roles of Dendritic Cells in the Immune System

3.1.1. Historical Background

Dendritic cells (DCs) are professional antigen-presenting cells (APCs) that play a central role in the initiation and regulation of immune responses. First identified by Ralph Steinman in 1972, DCs were subsequently recognized as key mediators linking innate and adaptive immunity (13, 14).

3.1.2. Origin and Development

DCs originate from bone marrow-derived hematopoietic stem cells and develop through a series of progenitor stages, including common myeloid progenitors (CMPs), monocyte-dendritic cell progenitors (MDPs), and common dendritic cell progenitors (CDPs). These progenitors ultimately give rise to the two major DC subsets: conventional dendritic cells (cDCs) and plasmacytoid dendritic cells (pDCs) (13).

3.1.3. Classification and Subtypes of Dendritic Cells

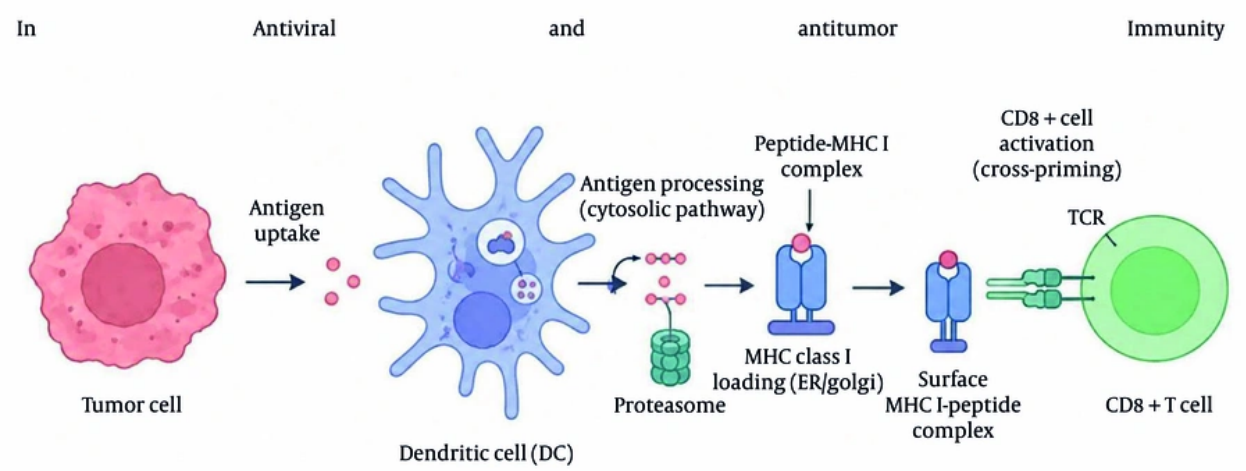

Figure 1. Mechanism of dendritic cell-mediated cross-presentation of tumor antigens. Following antigen uptake from tumor cells, dendritic cells process antigens and present peptide fragments on MHC-I molecules, thereby initiating $CD8^+$ cytotoxic T-cell responses through cross-priming (created using BioRender).

DCs comprise several functionally distinct subsets, including pDCs and cDCs, migratory DCs, and inflammatory monocyte-derived DCs (MoDCs). pDCs are major producers of type I interferons during antiviral responses, whereas the cDC1 and cDC2 subsets specialize in activating $CD8^+$ and $CD4^+$ T cells, respectively. Migratory DCs transport antigens from peripheral tissues to lymphoid organs, thereby facilitating T-cell priming and immune activation (13, 15-19).

3.1.4. Antigen Recognition, Uptake, and Presentation in Dendritic Cells

DCs play a key role in initiating immune responses by sensing pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs) through various pattern-recognition receptors (PRRs). These include Toll-like receptors (TLRs), C-type lectin receptors (CLRs), and NOD-like receptors (NLRs) (20-24). Upon encountering an antigen, DCs capture it via phagocytosis, macropinocytosis, and receptor-mediated endocytosis. After antigen uptake, DCs process it intracellularly and present it to T cells. Exogenous antigens are typically presented on MHC class II molecules to $CD4^+$ T cells, whereas intracellular antigens are presented on MHC class I molecules to $CD8^+$ T cells. Importantly, DCs can also perform cross-presentation, whereby exogenous antigens are presented on MHC class I molecules, thereby activating cytotoxic T lymphocytes and supporting antiviral and antitumor immunity (13, 20, 25) (Figure 1).

3.2. Types of Dendritic Cell-Based Vaccines

DC-based vaccines have been developed using multiple platforms, including autologous and allogeneic vaccines, peptide-loaded and neoantigen vaccines, DC/tumor fusion vaccines, exosome-based vaccines, and pDC-based vaccines, all aimed at improving antigen presentation and antitumor immunity.

3.2.1. Autologous vs Allogeneic Vaccines

Allogeneic dendritic vaccines, in contrast to the autologous approach based on cells derived from the patient, utilize DCs from healthy donors. This approach offers strategic advantages beyond facilitating mass production; in particular, the use of allogeneic cells can compensate for functional deficiencies in the immune cells of patients with cancer. Among allogeneic cell-based immunotherapy strategies, the GVAX vaccine occupies a special place. Although GVAX does not fit the classical category of dendritic vaccines, it effectively induces immune responses by using irradiated tumor cells genetically modified to express granulocyte-macrophage colony-stimulating factor (GM-CSF). This

vaccine facilitates antigen presentation and thereby T-lymphocyte stimulation by activating host dendritic cells. *Despite* the aforementioned manufacturing scalability advantages, immunological challenges, particularly the risk of graft rejection or treatment rejection by the host immune system, remain major obstacles (26, 27). Therefore, continued basic and clinical research is essential to optimize these therapeutic approaches.

3.2.2. Peptide-Loaded and Neoantigen Vaccines

The efficacy of DC-based vaccines depends not only on antigen selection but also on how antigens are loaded and presented via MHC pathways, and consequently on T-cell activation. Peptide vaccines have been widely studied because of their simple design and clinical applicability; however, they face limitations such as MHC haplotype dependence and limited stability of the peptide-MHC complex. To address these issues, long overlapping peptides were introduced, and neoantigen vaccines subsequently provided a more specific approach by targeting mutated tumor antigens. In recent years, engineered systems and combinations of these vaccines with immune checkpoint inhibitors have been proposed as strategies to improve antitumor responses (28, 29).

3.2.3. DC/Tumor Fusion Vaccines

In contrast to peptide-loading techniques, tumor immune escape is less likely with this approach because tumors can suppress the expression of specific antigens used in peptide-based vaccines. DC/tumor hybrid vaccines are produced by mixing dendritic cells and tumor cells, generating hybrid cells that combine the antigen-presenting capacity of DCs with a complete range of TAAs. These hybrid cells can effectively stimulate tumor-specific killer T cells because they express MHC class I and MHC class II receptors as well as co-stimulatory receptors. Compared with peptide vaccine strategies, the likelihood of tumor immune escape is minimized because antigen presentation can be performed by the hybrid cells. After fusion, TAAs are processed within the hybrid cells through MHC class I and II pathways (28, 30).

3.2.4. DC-Derived Exosome Vaccines

Exosomes are extracellular vesicles released by the fusion of multivesicular bodies (MVBs) with the plasma membrane. Dendritic cell-derived exosomes (Dex), approximately 30 - 150 nm in size, can carry peptide molecules along with MHC and co-stimulatory molecules and contribute to immune induction. These vesicles carry immunogenic molecules such as MHC class I and II and surface antigens including CD1, CD36, and neuropilin-1, while also carrying complement regulatory proteins such as CD55 and CD59, which contribute to their stability in circulation. Unlike DCs, the primary role of Dex is more in antigen transfer than in direct presentation; however, they can stimulate $CD4^+$ and $CD8^+$ T cells as well as NK cells and, owing to their cell-free nature, may partially bypass the limitations imposed by tumor immunosuppression (28, 31).

3.2.5. pDC-Based Vaccines

pDCs represent a specialized subset of dendritic cells that contribute to immune surveillance and host defense, largely through their strong capacity to produce type I interferons. In peripheral blood and lymphoid tissues, they are typically identified by expression of CD123, BDCA-2 (CD303), and BDCA-4 (CD304). Beyond interferon production, pDCs also influence immune responses through secretion of cytokines and chemokines such as IL-6, IL-12, TNF-α, and CXCL10, which collectively support NK- and T-cell activation. Although initially considered less efficient APCs than classical dendritic cells, it is now well established that they can present antigens to both $CD4^+$ and $CD8^+$ T cells. In addition, activated pDCs may exhibit direct cytotoxic activity via TRAIL and granzyme B (28, 32). Overall, pDCs display considerable functional plasticity, acting as immune enhancers or regulators depending on the TME, highlighting their relevance in cancer.

3.3. Design and Production of DC Vaccines

3.3.1. Monocyte Differentiation Into DCs

Peripheral blood monocytes represent the most commonly used source for generating DC-based vaccines. These cells account for approximately 10% of peripheral blood mononuclear cells and can be isolated using magnetic bead separation or leukapheresis (33). In the standard differentiation protocol, monocytes are cultured with GM-CSF and IL-4 for five to seven days (34).

GM-CSF promotes myeloid differentiation, whereas IL-4 suppresses macrophage development and supports DC lineage commitment. Successful differentiation is typically characterized by loss of CD14 and acquisition of DC markers such as CD1a and CD11c, resulting in immature DCs with low expression of maturation markers (35).

Although MoDCs remain the most widely used platform in clinical trials because of scalability and compatibility with cryopreservation, increasing attention has been directed toward natural DC subsets such as cDC1 and cDC2 because of their superior antigen cross-presentation capacity (36). Cryopreserved DC vaccines have demonstrated high viability (82 - 99%) even after long-term storage, while maintaining phenotypic stability and sterility within batch-release criteria (37).

3.3.2. Antigen Loading Strategies

After maturation, immature DCs must be loaded with TAAs to ensure efficient priming of T cells. Several antigen-loading approaches have been identified, including peptide loading, tumor lysate, apoptotic tumor cells, and delivery of nucleic acids encoding TAAs (36).

Peptide antigens (8 - 11 amino acids) predominantly mediate processing and presentation by MHC class I molecules, leading to $CD8^+$ T-cell activation, whereas peptides 15 - 30 amino acids in length can be processed by both MHC class I and II molecules and consequently stimulate $CD8^+$ and $CD4^+$ T cells (33). Use of tumor lysate enables loading with a broad variety of known and unknown antigens but requires intracellular processing, and apoptotic tumor cell loading allows loading with both intracellular and membrane-associated tumor antigens (36).

Nucleic acid-based strategies use the endogenous protein synthesis machinery of DCs to produce tumor antigens. Techniques such as mRNA electroporation or viral vector-mediated transduction enable efficient antigen expression. mRNA electroporation is widely used because of its high transfection efficiency and lack of genomic integration risk, whereas viral vectors provide prolonged antigen expression but raise additional safety considerations (38, 39).

3.3.3. Maturation and Activation Signals

Antigen loading alone is insufficient to generate immunogenic DCs, as immature DCs may induce immune tolerance rather than effective T-cell activation. Therefore, maturation signals are required to enhance co-stimulatory molecule expression, cytokine production, and lymph node migration. Early DC-based vaccines used immature DCs, whereas second-generation approaches employed cytokine cocktails such as TNF-α, IL-1β, IL-6, and PGE_2 to induce maturation (34).

A major advancement was the development of the α-type-1 polarization cocktail described by Kalinski and colleagues. This formulation includes poly I:C (a TLR3 agonist), TNF-α, IL-1β, IFN-α, and IFN-γ and promotes expression of CCR7, CD80, and CD86 while enhancing the ability of DCs to produce IL-12p70, a cytokine critical for CTLs (34).

More recently, another study has demonstrated that specific TLR agonists, including CpG, poly I:C, LPS, and R848, can further optimize DC activation in cDC subsets (40). Building on these advances, the zDC platform combines sequential stimulation with poly I:C followed by R848 and α-type-1 cytokines, resulting in markedly increased IL-12p70 production, improved migration capacity, and enhanced induction of CTLs (34) (Figure 2).

3.4. Mechanisms of DC Vaccines Against Tumors

3.4.1. Overview of DC-Based Vaccine Mechanisms

Cancer vaccines are designed to stimulate the immune system to recognize and kill tumor cells, and DCs are the most effective antigen-presenting cells for activating naïve T cells (29). In DC-based vaccination, ex vivo differentiation of patient-derived monocytes into DCs is followed by loading with tumor antigens, maturation, and infusion to enable migration to lymph nodes, where they activate T cells through MHC-mediated antigen presentation. T-cell activation is contingent on three discrete signals that coordinate antigen presentation (signal 1), co-stimulation via CD80/CD86 (signal 2), and cytokine-driven polarization (signal 3) (41). This three-signal model provides the foundation for DC vaccine design; however, tumor-induced immunosuppression can impair all three signals, thereby affecting overall therapeutic efficacy.

3.4.2. Activation of $CD8^+$ Cytotoxic T Lymphocytes

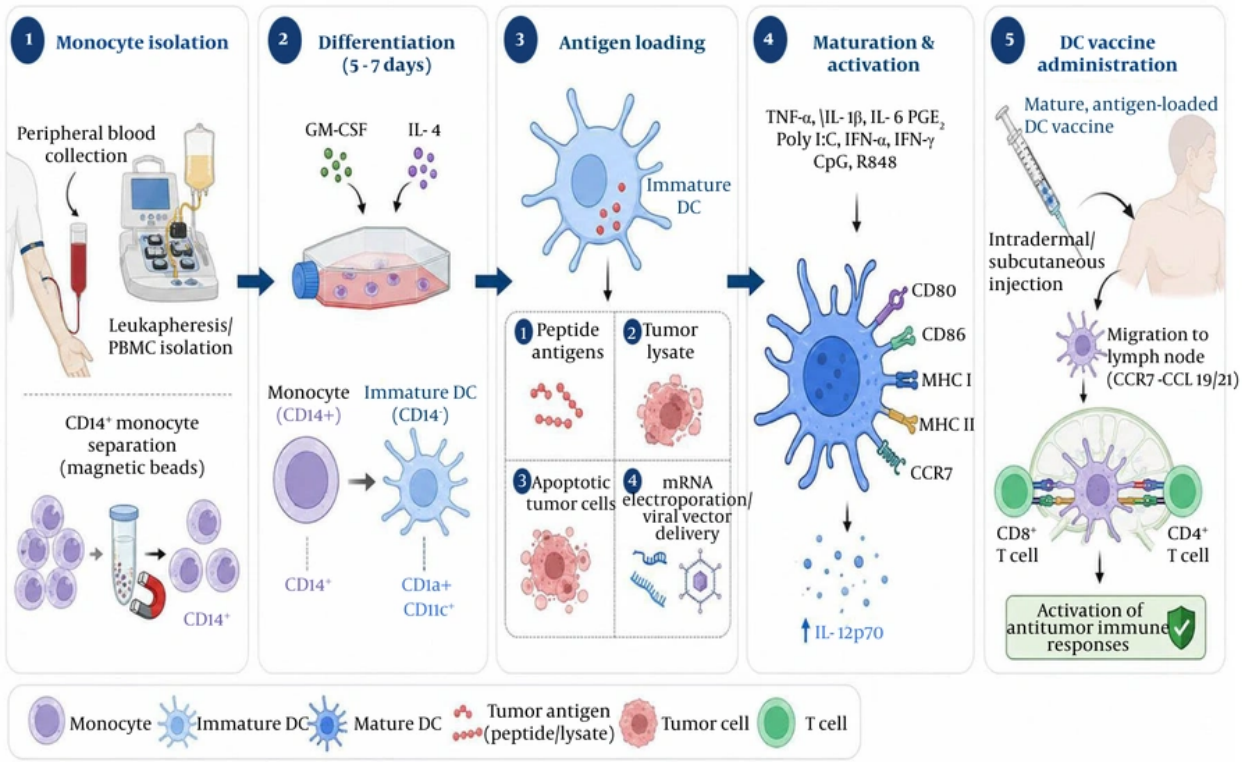

Figure 2. Schematic image of monocyte-derived dendritic cell (MoDC) vaccine generation and preparation. The workflow illustrates: (1) isolation of CD14 + monocytes from patient PBMCs, (2) cytokine-driven differentiation (GM-CSF/IL-4) into immature DCs, (3) tumor antigen loading using alternative strategies, (4) cocktail-induced maturation and activation (characterized by upregulated CCR7, MHC, and costimulatory molecules), and (5) therapeutic administration to trigger CD4 +and CD8 + T-cell-mediated antitumor immunity.

A key objective of DC-based vaccination is to stimulate the generation of CTLs, which have the ability to specifically eradicate autochthonous tumor cells that present antigen via cross-presentation on MHC class I-expressing molecules. Two dominant modes of cross-presentation have been identified: the vacuolar pathway (antigen processing occurs in endosomal compartments) and the cytosolic pathway (in which antigens transiently enter the cytoplasm, are degraded by proteasomes, and are then loaded onto MHC class I through TAP-dependent transport). Recent studies reported the identification of SEC22B, a key regulator that enables ER-phagosome fusion and cross-presentation efficiency (25). At the top of the DC subset hierarchy, cDC1s are exceptionally efficient cross-presenters that outperform cDC2s in eliciting antitumor $CD8^+$ T-cell responses (40). Strategies to enhance this function include overexpression of CCR7 to promote migration, CD40L expression to enhance T-cell stimulation, and targeting of the m^6A reader YTHDF1, which not only reduces antigen degradation but also increases cross-presentation efficiency (39, 42). Collectively, these strategies aim to enhance DC-mediated delivery of potent $CD8^+$ antitumor immunity.

3.4.3. Activation of $CD4^+$ Helper T Cells

$CD8^+$ T cells require $CD4^+$ T-cell help for optimal priming (43, 44), which is mediated through DCs via a two-step licensing model. In this process, $CD4^+$ T cells first recognize antigen on DCs and subsequently induce CD40L-CD40 interactions, thereby licensing DCs to enhance $CD8^+$ T-cell activation, even against distinct antigens presented on the same DC. CD40 signaling increases IL-12 production, upregulates co-stimulatory

molecules (CD80, CD86, CD70), and activates NF-κB-dependent inflammatory pathways. CD70 further engages CD27 on $CD8^+$ T cells, promoting clonal expansion and preventing T-cell exhaustion (45). DC subset composition also critically influences this process, as cDC1-driven responses preferentially induce robust Th1 $CD4^+$ T-cell populations producing IFN-γ, TNF-α, and IL-2, thereby supporting cytotoxic T lymphocyte expansion and function (40).

3.4.4. Induction of Immunological Memory

In addition to triggering effector responses, DC-based vaccination can help establish long-term immunological memory. Activated $CD4^+$ helper and $CD8^+$ cytotoxic T cells develop into memory T-cell pools that can rapidly reactivate upon re-encounter with the same antigen (40). cDC1s are especially effective at promoting both effector and memory $CD8^+$ T-cell responses because of their superior antigen-presentation capacity (40, 25). In addition, emerging genetic engineering methods, such as CRISPR editing and RNA interference, have been investigated to improve antigen presentation and strengthen the durability of T-cell memory responses (38).

3.4.5. Interaction With the Tumor Microenvironment

Despite their therapeutic potential, the efficacy of DC vaccines is frequently limited by the TME, which contains multiple immunosuppressive components (46). Regulatory T cells (Tregs), myeloid-derived suppressor cells (MDSCs), and inhibitory signaling pathways, including programmed death-ligand 1 (PD-1/PD-L1), contribute to suppression of immune responses (46, 47). MDSCs can inhibit T-cell proliferation, impair DC maturation, and reduce antigen presentation efficiency. In addition, altered chemokine expression within tumor tissues may restrict T-cell trafficking and infiltration, leading to reduced antitumor activity (48).

3.4.6. Synergy With Other Immunotherapies

Combining DC-based vaccines with other forms of immunotherapy may improve efficacy. Immune checkpoint inhibitors, such as antibodies blocking PD-1/PD-L1, can help reverse immune suppression and enable improved immune cell function (49). In addition, manipulation of chemokine pathways and genetic modification techniques may support the recruitment and activation of immune cells (48, 38).

3.5. Clinical Evidence

3.5.1. Organ-Specific Clinical Evidence

3.5.1.1. Melanoma

Melanoma is a cancer type formed by melanocytes. Unlike many other skin cancers, malignant melanomas can migrate to other organs such as the lymph nodes. In addition to being one of the most lethal forms of skin cancer worldwide, melanoma remains difficult to treat with existing modalities. Detailed outcomes of reviewed clinical trials are summarized in Table 1.

In recent years, DC-based vaccinations, particularly autologous vaccines, have been investigated as an immunotherapy for advanced or high-risk melanoma. These vaccines were generated from natural DC subtypes or moDCs and, in most investigations, were loaded with autologous tumor lysate or melanoma-associated antigens such as MART-1, gp100, tyrosinase, MAGE-A3, and NY-ESO-1. Enhanced antitumor-specific responses, including increased antigen-specific CD8+ responses, IFN-γ production, DTH responses, Th1 activation, induction of multifunctional T cells, and occasionally epitope spreading, have been reported in numerous immunological studies. These findings suggest that DC-based vaccinations can stimulate the immune system to recognize melanoma antigens; however, the strength and duration of these responses have varied across investigations (56-66, 68, 70-78, 81-90).

Despite significant immunogenicity, the clinical efficacy of DC vaccines in melanoma has been heterogeneous. Some studies, particularly in stage III/IV patients with resected or clinically unresectable disease, have reported improvements in DFS, RFS, or overall survival, whereas other trials have shown limited objective responses or unclear clinical benefit. These differences are likely related to factors such as disease stage, tumor burden, antigen type and source, DC phenotype and maturation method, route of administration, HLA status, quality of the cell product, adjuvants used, and patient immunosuppression status (50, 60, 64, 65, 66, 69, 76, 79, 81).

The MIND-DC phase III trial by Bol et al. (2024) tested adjuvant dendritic cell therapy in patients with stage IIIB/C melanoma, showing that DC-based vaccination

was safe and could stimulate robust tumor-specific T-cell immune responses, yet did not improve recurrence-free survival compared with standard follow-up (85). This trial is significant because it illustrates a major challenge of DC-based cancer vaccines: immune responses do not always translate into clinical benefit.

Hodi et al. evaluated the WDVAX vaccine as a biomaterial-based cancer vaccine platform in patients with metastatic melanoma in a controlled phase 1 trial. The vaccine consisted of a macroscopic and microporous polylactide-co-glycolide/PLG scaffold loaded with three key components: autologous tumor lysate (a broad source of tumor-specific and associated antigens), GM-CSF (to attract and accumulate dendritic cells and other APCs at the implant site), and G oligodeoxynucleotide (a TLR9 agonist to induce dendritic cell maturation and activation). A key aspect of this study is that WDVAX uses a biodegradable scaffold to attract, antigen-load, and activate the patient's own DCs in vivo, rather than generating dendritic cells ex vivo (86). Therefore, this approach can be considered a new generation of cancer vaccines within the framework of immunoengineering.

A novel approach in melanoma treatment is the combination of DC-based vaccines with TIL-ACT. In a phase I trial, this approach was investigated in patients with metastatic melanoma who had progressed after treatment with immune checkpoint inhibitors. In the reviewed study, TIL treatment was first administered alone to assess safety and optimize the regimen, and then TIL was evaluated in combination with an autologous DC vaccine loaded with tumor lysate. In the combination group, all four evaluable patients had objective responses; two achieved complete responses and two achieved partial responses, and in some patients the responses were sustained for more than 42 months. Long-term persistence of the injected TILs in the blood was also confirmed (87). These findings suggest that DC vaccines can enhance and maintain antitumor responses after TIL transfer by continuously stimulating antigen.

Overall, DC-based vaccines in melanoma are promising in terms of safety and immunological activity, but achieving sustained clinical benefit requires more careful patient selection, optimization of DC type, antigen source, and production methods, and rational combination with checkpoint inhibitors.

3.5.1.2. Glioblastoma

Despite recent advances, GBM remains the most malignant brain tumor and is characterized by poor prognosis, as fewer than 25% of cases survive for more than a year after diagnosis. Detailed outcomes of reviewed clinical trials are summarized in Table 2.

Liau et al. (2023) reported one of the most important clinical studies of DC-based vaccines in glioblastoma through the DC Vax-L trial. In this phase III study, patients with newly diagnosed glioblastoma who received autologous tumor lysate-loaded DC-based vaccines showed longer median overall survival compared with matched external control populations. The vaccine was also well tolerated, with few serious treatment-related adverse effects (113). This study strengthened the idea that DC-based vaccines may improve survival in highly aggressive tumors such as glioblastoma, although the use of external controls instead of a fully randomized comparison remains a major limitation frequently discussed in the field.

In a randomized pilot trial in patients with newly diagnosed GBM, the addition of a DC-based vaccine loaded with CMV pp65 antigen RNA to adoptive transfer of pp65-specific T cells resulted in a significant increase in CMV-specific polyfunctional $CD8^+$ T cells capable of producing IFNγ, TNFα, and CCL3. This increase was positively correlated with overall survival ($R = 0.7371$, $P = 0.0369$), although a definitive causal relationship could not be inferred (114). Therefore, this study suggests T-cell polyfunctionality as a potential biomarker of response to immunotherapy and supports DC vaccines as components of combination strategies in GBM.

Akasaki et al. (115) conducted a clinical trial in patients with GBM to investigate the effectiveness of combination therapy using chemotherapy with TMZ and immunotherapy based on hybrid cells generated by fusion of DCs and gliomas. In this approach, patients received intradermal injections of autologous glioma cells mixed with autologous DCs. The technique was tolerated by all participants and was associated with progression-free survival and overall survival benefits. In addition, the study noted elevated CAPs expression in recurrent tumors and induction of immune responses to the antigens, as confirmed by immunological tests (115). These findings suggest that combining TMZ with a DC-glioma cell fusion-based vaccine can yield notable

antitumor effects through immune responses against drug-resistance antigens.

Most trials have used autologous DCs loaded with tumor lysates, tumor-specific antigens, synthetic peptides, or tumor stem cells. Results indicate that DC vaccination can induce specific immune responses, increase cytotoxic T lymphocyte activity, and enhance immune-cell infiltration into the tumor, which plays an important role in the development of antitumor immunity (88-95).

With respect to vaccine type, studies have used varying strategies. In some studies, vaccines were produced by presenting whole tumor lysates to dendritic cells, thereby providing a broad selection of tumor antigens. Other strategies used individual tumor antigens such as WT1 or EGFRvIII or multiple tumor peptides. In many cases, the vaccine strategy targeted antigens expressed on tumor-initiating or tumor stem cells implicated in disease recurrence or therapy failure. These results suggest that DC vaccines can elicit measurable immune responses in some patients, such as augmentation of tumor antigen-specific T cells, IFN-production, or skin test responses; however, clinical outcomes have been heterogeneous and appear to depend on antigen type as well as patient HLA type and tumor properties (94, 96-98, 101, 106, 108, 110, 113, 117).

Some studies have shown that patients with characteristics such as MGMT methylation, specific IDH1 or TERT status, low B7-H4 expression, higher infiltration of $CD8^+$ cells into the tumor, or a lower $PD\text{-}1^+/CD8^+$ ratio may respond better. Conversely, combining DC vaccines with immune boosters such as poly-ICLC, resiquimod, or CMV pp65-targeted vaccines has enhanced immune responses (88, 94, 98, 99, 101, 103, 109, 110, 112).

In conclusion, the available evidence suggests that dendritic cell vaccines in glioblastoma are defensible in terms of safety and biological rationale; however, larger, more controlled studies with more careful patient selection are still needed to definitively demonstrate effects on survival.

3.5.1.3. Prostate Cancer

Prostate cancer is the most common cancer in men in more than half of all nations, with approximately 1.4 million cases each year. Detailed outcomes of reviewed clinical trials are summarized in Table 3.

DC-based vaccines have shown a favorable safety profile across a wide range of prostate cancer stages, from biochemical relapse to castration-resistant disease. Most studies successfully induced measurable cellular immune responses, including antigen-specific CD8+ activity, DTH responses, and ELISpot responses against antigens such as PSA, PSMA, PSCA, Survivin, and MUC1. The most frequent positive clinical observation was an increase in PSA doubling time, indicating slower biochemical progression, whereas objective tumor responses were uncommon and inconsistent. Several studies demonstrated a significant correlation between the strength of the induced immune response and improved clinical outcomes, including longer survival and a lower risk of relapse (116-133). Taken together, these results confirm the immunogenic potential of DC-based vaccines; however, improved patient selection, standardization of DC products, and development of targeted combination regimens are necessary to achieve meaningful clinical benefit.

Sipuleucel-T received regulatory approval from the FDA on April 29, 2010, becoming the first personalized cellular immunotherapy indicated for the treatment of advanced prostate cancer (134). Across studies of Sipuleucel -T, this autologous cellular immunotherapy, generated from APCs activated with the PAP-GM-CSF fusion protein and the first approved immunotherapy for mCRPC, demonstrated a reduction in the risk of death of approximately 22 - 33% and an improvement in median overall survival of approximately 4 months compared with placebo (135-137). Immunological studies have shown that this therapy induces antigen-specific cellular and humoral responses, and the degree of APC activation, cell number, and intensity of the immune response were significantly correlated with survival (138-140). Evidence suggests that Sipuleucel -T induces long-lasting immune memory, increases TCR diversity in prostate tissue, and delayed clinical responses, including PSA declines several months after completion of treatment, have been observed in some patients (141, 142). The combination of Sipuleucel -T with checkpoint inhibitors such as ipilimumab and atezolizumab was safe and tolerable, but did not show significant improvements in immune responses or clinical outcomes compared with monotherapy (143, 144). Collectively, these findings support the immunogenic potential and survival benefit of Sipuleucel -T, although optimization of combination regimens and

identification of predictive biomarkers remain essential.

A phase I trial evaluated the safety and efficacy of a novel cell-based vaccine, BPX101, in men with mCRPC. In this approach, autologous APCs were loaded with an engineered adenoviral vector and the target antigen PSMA to enhance tumor-specific immune responses. These cells contained an inducible CD40 receptor activated by the dimerizing drug rimiducid, allowing temporal control of dendritic cell activation. Results showed that this treatment had limited side effects and, in addition to activating the immune system, resulted in PSA reduction and even tumor regression in some patients (119). This targeted immunotherapy platform may be a promising option for further development, either as monotherapy or in combination with other therapies.

The phase III VIABLE trial in patients with metastatic castration-resistant prostate cancer (mCRPC) showed that adding DCVAC/PCa, an autologous active cellular immunotherapy, to docetaxel/prednisone followed by maintenance therapy did not improve overall survival. In this randomized, double-blind, placebo-controlled study, median overall survival was 23.9 months with DCVAC/PCa versus 24.3 months with placebo (HR=1.04; P = 0.60), and no differences were observed in secondary endpoints, including radiological progression-free survival, time to PSA progression, and skeletal-related events (145). The treatment was generally well tolerated but did not demonstrate significant antitumor efficacy.

Ager, C. R. et al. in 2026 suggested that treatment with BMS-986218 + ADT, in addition to reducing Treg, altered function and increased the abundance of dendritic cells (DCs) in the tumor environment. The reduction of Tregs was accompanied by increased activity and number of DCs, leading to enhanced priming of T cells and a more effective immune response against the tumor (146).

3.6. Phase III Clinical Trials

Among published clinical trials of dendritic cell-based immunotherapy, only a limited number have successfully entered phase III. Studies in melanoma, glioblastoma, and prostate cancer have provided key evidence regarding efficacy, safety, and impacts on clinical outcomes. A summary of the most important phase III studies is presented in the table below (Table 4).

3.7. Safety and Side Effects

3.7.1. Melanoma Studies

DC-based vaccines for melanoma have generally shown a manageable safety profile across clinical trials, although adverse effects have been reported at varying levels. The most commonly observed clinical side effects include mild injection-site reactions, flu-like symptoms, and post-infusion chills (67, 69), with transient enlargement of draining lymph nodes noted particularly after intradermal administration (58). Vitiligo, reflecting cutaneous autoimmunity, emerged in a subset of patients across separate studies (64, 77), and one trial recorded an iatrogenic pneumothorax as the sole grade 3 treatment-related adverse event (61). More concerning, however, are immunological side effects that may be less apparent clinically. Following DC vaccination, a notable upregulation of PDL1+ tumor cells was observed, representing adaptive immune resistance that allows the tumor to counter vaccine-induced immune activation (52). In parallel, expansion of regulatory T cells (CD4+CD25+) and elevated IL-10 secretion were found to dampen antitumor immune responses (54), and local CpG administration unexpectedly drove higher FoxP3 and CTLA4 expression in Tregs within the sentinel lymph node, amplifying suppressive activity (72). In patients receiving GM-CSF, a paradoxical reduction in circulating dendritic cells and development of GM-CSF neutralizing antibodies were also documented (73). Taken together, while acute serious toxicity remains uncommon (59, 63, 76, 84), a key challenge is the immunological counterresponses that these vaccines can inadvertently provoke, which may ultimately blunt therapeutic potential.

3.7.2. GBM Studies

DC-based vaccines in glioblastoma have generally shown an acceptable safety profile. The most common clinical side effects included local injection-site reactions and flu-like symptoms (102), and in one study, transient and reversible elevations of liver enzymes AST/ALT were observed in nearly half of patients (96). More serious side effects were rare; cerebral edema was reported in one patient (89), and seizures were reported in some cases, leading to treatment discontinuation (102). At the immunological level, an unintended increase in Treg after treatment was documented as a

Table 4. Summary Outcomes of Phase III Trials

Cancer Types	Vaccine Name	Overall Survival Benefit (OS)	Progression-Free Survival Benefit (PFS)	Regulatory; Approval
Melanoma (stage IV); (76)	Autologous peptide-loaded dendritic cell vaccine vs dacarbazine	No	No	No
Melanoma (resected stage IIIB/C) 91	MIND-DC	No	No	No
Glioblastoma; (113)	DCVax-L	Yes	Not reported / No clear benefit	Approved in UK,not FDA/EMA approved
Prostate cancer; (135)	Sipuleucel-T	Yes	No	Yes
prostate cancer; (137)	Sipuleucel-T / APC8015	Yes	No	Yes
Prostate cancer; (145)	DCVAC/PCa + docetaxel/prednisone	No	No	No

side effect that inhibited antitumor immune responses (110). In the largest trial conducted, only 2.1% of patients experienced grade 3 - 4 adverse events associated with the DCVax-L vaccine (101).

3.7.3. Prostate Cancer Studies

DC-based vaccines have shown a more favorable safety profile in prostate cancer than in other cancers. The most commonly reported clinical adverse events were mild injection-site reactions and transient flu-like symptoms such as fever, chills, and headache; these were mostly grade 1 - 2 and lasted for 1 - 2 days (133, 135, 136). In a combination study with atezolizumab, 83.8% of patients experienced at least one treatment-related event, although immune and infusion reactions were all grade 1 - 2, and no grade 4 or 5 toxicities were observed (144). At the immunological level, increased IL-10 levels have been noted in some patients as an immunosuppressive side effect (121), and decreased TCR sequence diversity in peripheral blood after Sipuleucel-T suggests a rearrangement of the T-cell repertoire, the clinical consequences of which remain unclear (141). A key negative finding is the failure of DCVAC/PCa in the largest phase III trial; despite good tolerability, no overall survival advantage was observed versus placebo (145), highlighting that a favorable safety profile does not necessarily translate into clinical efficacy.

3.8. Limitations and Future Directions

3.8.1. Limitations

3.8.1.1. Melanoma Studies

Interpretation of DC vaccine trials in melanoma is limited by methodological, biological, and technical challenges. Most studies are small phase I/II trials with fewer than 30 patients per arm (67, 68, 79, 82), often lacking randomized or blinded controls and inadequately accounting for confounding factors such as checkpoint inhibitor therapy and G-CSF administration (52, 57, 64, 72, 79). Moreover, clinical outcomes are often not correlated with vaccine-elicited immune responses (53, 56, 71, 74), and no single immunological biomarker has been established as predictive of survival (74, 84). Analyses of tumor tissues have identified immunosuppressive mechanisms, such as PD-L1 upregulation and increased expansion of Tregs and MDSCs, that could inhibit vaccine-primed T-cell activity (53, 73). Additional variability arises from inconsistencies in DC manufacturing and maturation status (57, 76), as well as the potential mismatch between peptides presented by vaccine DCs and those expressed by melanoma cells (54). Together with premature trial closures due to slow accrual, funding limitations, and the emergence of checkpoint inhibitors (50, 62, 67), and the lack of positive phase III evidence beyond the negative DeCOG trial (76), these limitations hinder definitive assessment of the clinical efficacy of DC vaccination in melanoma.

3.8.1.2. GBM Studies

Methodological and biological hurdles affect the interpretation of DC vaccine trials in glioblastoma. Most studies are small phase I/II trials, and single-arm designs or inadequate randomization limit statistical power, while selection bias is a genuine risk (88-90, 103, 104). Vaccine-induced immune responses are often not associated with survival (94, 105, 111), likely because peripheral immune monitoring does not correlate well with the highly immunosuppressive glioblastoma microenvironment, as reflected by multiple factors including regulatory T cells, myeloid-derived suppressor cells, or B7-H4 expression (88, 109). Vaccine manufacturing (92), tumor tissue or monocyte deficiencies (97), and the confounding effects of corticosteroids, temozolomide, bevacizumab, and pseudo-progression on MRI interpretation further

complicate clinical interpretation of findings (104, 105). Collectively, these limitations impede clear conclusions regarding the clinical utility of DC vaccination in glioblastoma.

3.8.1.3. Prostate Cancer Studies

Most prostate cancer DC vaccine trials are limited by small sample sizes and single-arm designs, with few randomized studies and insufficient power to draw definitive conclusions regarding survival outcomes (117, 121, 127, 129, 131). A consistent limitation is the weak correlation between immune readouts (e.g., DTH, T-cell proliferation, IFN-γ production) and clinical endpoints such as PSA decline or survival (117, 122, 127, 130). PSA kinetics may also be confounded by non-treatment-related fluctuations, including transient PSA rises that mimic progression (131). Patient selection further restricts efficacy, as most trials enroll heavily pretreated, immunocompromised patients with impaired T-cell function (117, 118). In addition, substantial variability in DC manufacturing, including differences in maturation state and tolerogenic phenotypes (CD14, IL-10), is often not controlled for (118). Collectively, these limitations hinder robust assessment of DC vaccine efficacy in prostate cancer.

3.8.1.4. Economic and Manufacturing Challenges

The clinical translation of dendritic cell (DC)-based vaccines is limited by substantial economic and logistical barriers in addition to biological constraints. Autologous DC production requires labor-intensive ex vivo culture in specialized GMP facilities and relies on costly cytokines and maturation cocktails (e.g., GM-CSF, IL-4), with multi-day processing times. The estimated cost per patient ranges from $50,000 to $100,000 per treatment course, excluding hospitalization and administrative expenses (29). Although cryopreservation of final products is feasible, it increases procedural complexity and expense (37). Further challenges include inter-batch variability in DC maturation and antigen loading, as well as the lack of widely available standardized manufacturing infrastructure outside specialized academic centers. Collectively, these constraints, together with modest efficacy signals in late-phase studies, have limited the clinical adoption of DC vaccines in malignancies such as melanoma and glioblastoma.

3.8.2. Future Directions

Despite these limitations, the future of the field will likely depend on the development of combinatorial therapies. Such approaches seek to combine classical strategies with personalized vaccines containing tumor neoantigens encoded by patients' mRNAs and ICIs. In addition, the use of immunostimulants is expected to play a critical role in the success of these approaches. It will be necessary to move beyond existing procedures by not only increasing intervention frequency but also improving product quality and developing predictive biomarkers.

4. Conclusions

DC-based vaccines have generally demonstrated a favorable safety profile in clinical studies and can induce specific antitumor immune responses. However, most phase III trials, including MIND-DC in melanoma and VIABLE in prostate cancer, have not shown significant improvement in survival outcomes. A notable exception is Sipuleucel-T, the only FDA-approved dendritic cell-based vaccine, which has been associated with a meaningful reduction in the risk of death in prostate cancer. Overall, despite their clear immunological potential, current evidence remains insufficient to confirm consistent clinical efficacy, and further optimization of treatment strategies and combination approaches appears necessary.

Footnotes

AI Use Disclosure: ChatGPT was used in generating images.

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Table 1. Summarized Data from Clinical Studies (DC-Based Vaccines for the Treatment of Melanoma Cancer)

Authors (y)	Main Objective	Stage of disease	Cell type used	conclusion
Bulgarelli et al. (50); (2025)	Evaluate the safety and immune activity of autologous DC vaccination as adjuvant therapy in resected stage III/IV melanoma	Resected Stage III/IV melanoma	Autologous DCs	Induces immunological activity; May improve relapse-free survival (RFS)
Ribas et al. (51); 2004	Further characterize the immune activity of MART-1 peptide-pulsed DC vaccine and assess its link with determinant spreading	Stage II-IV melanoma	Autologous ex vivo generated immature DC pulsed with MART-1 (23, 24, 25, 26, 27, 28, 29, 30) peptide	The vaccine induced immunologic activity.; Determinant spreading may indicate an effective antitumor response.; DC phenotype and cytokine profile did not correlate with T-cell induction.; Clinical efficacy remains uncertain.; Sequential CTLA-4 blockade may enhance immune effects.
Oshita et al. (52); 2012	Evaluate the efficacy of a peptide-pulsed dendritic cell vaccine in metastatic melanoma (mainly HLA-A24)	Metastatic melanoma (mostly chemo resistant)	Autologous DCs pulsed with a 5-peptide melanoma antigen cocktail (gp100, tyrosinase, MAGE-A2, MAGE-A3, MART-1/MAGE-A1) + KLH	Peptide-pulsed DC vaccination induced strong anti-tumor immune responses.; Immune response markers correlated with better prognosis.; DC vaccination was associated with a significant prolongation of overall survival in metastatic melanoma.
Bulgarelli et al. (53); 2019	Evaluate TNE changes after DC vaccination in metastatic melanoma	Melanoma metastatic	Autologous DC loaded with tumor lysate/homogenate	DC vaccination "heated up" the TME.; But tumors simultaneously upregulated PD1, causing adaptive resistance.; This supports DC vaccine + checkpoint inhibitor combination strategies.
Dannull et al. (54); 2013	Evaluate whether DCs engineered to process antigens via constitutive proteasomes (cPs) improve anti-melanoma immune responses	Metastatic melanoma	Monocyte-derived mature DC transfected with RNA encoding melanoma antigens (MART-1, MAGE-3, gp100, tyrosinase)	CP-engineered DCs generated stronger and more durable antigen-specific T-cell responses.; They reduced circulating melanoma cells and induced tumor-specific cytotoxicity.; Only the CP-engineered group showed clinical responses (1 PR, 1 CR), suggesting enhanced therapeutic efficacy.
Chakraborty et al. (55); 2004	To evaluate how $CD4^+$ T-regulatory cells influence antitumor CTL responses after vaccination with peptide- or tumor lysate-loaded APC/DC vaccines in melanoma patients	Melanoma cancer	Autologous APC/DCs loaded with MART-1 (23, 24, 25, 26, 27, 28, 29, 30), MAGE-1 (161 - 169) peptides, or autologous tumor lysate	Vaccination induced a transient expansion of antigen-specific CTLs in peripheral blood.; This CTL response subsequently declined in parallel with an expansion of $CD4^+CD25^+$ T cells.; Findings indicate that CD4+CD25+ regulatory T cells can down-modulate vaccine-induced antitumor CTL responses.
Lesterhuis et al. (56); 2011	To compare wild-type vs. modified gp100 peptides (with higher MHC class I affinity) for DC loading in advanced melanoma vaccination	Metastatic melanoma ($HLA\text{-}A2.1^+$)	Autologous mature DCs loaded with KLH, tyrosinase peptide, and either wild-type or modified gp100 peptides	Both wild-type and modified peptide vaccines were similarly immunogenic.; Only 3 patients developed detectable gp100-specific T cells; Two long-term complete responses occurred (one in each group), indicating no clear benefit from peptide modification.
Schreibelt et al. (57); 2016	To evaluate the feasibility, safety, and immune efficacy of vaccination with primary circulating CD1c(+) myeloid DCs in stage IV metastatic melanoma patients	Stage IV metastatic melanoma, treatment-naïve for metastatic disease	Autologous primary CD1c(+) myeloid DCs, briefly activated ex vivo and loaded with tyrosinase and gp100 antigens	Vaccination induced multifunctional $CD8^+$ T-cell responses with cytolytic activity (e.g., high CD107a, IFNγ, TNFα).; Primary myeloid DC vaccination is feasible, safe, and promotes effective anti-tumor immunity linked to clinical benefit.
Escobar et al. (58); 2005	To evaluate toxicity, immunological, and clinical responses of autologous DCs pulsed with melanoma cell lysate alone or combined with low-dose IL-2 in stage III/IV melanoma patients	Stage III or IV malignant melanoma	Autologous monocyte-derived DCs pulsed with melanoma cell lysate	50% patients showed increased IFN-γ responses, confirming immune activation.; Positive delayed-type hypersensitivity (DTH) correlated with disease stability and survival.; Combination with IL-2 did not significantly enhance responses; vaccination alone is safe and partially effective.
Chang et al. (59); 2009	To evaluate the efficacy and safety of autologous melanoma apoptotic bodies (MAB)-pulsed DCvaccination in metastatic melanoma patients	Metastatic refractory melanoma	Autologous monocyte-derived DCs pulsed with melanoma apoptotic bodies (MAB)	MAB-pulsed DC vaccine showed modest efficacy: 1 partial response, 2 stable disease > 24 months.; Delayed-type hypersensitivity to KLH was consistent; no DTH to tumor antigens.; Safe but limited clinical benefit; suggests need for combination with other therapies.
Vreeland et al. (60); 2021	To evaluate safety and efficacy of tumor lysate particle-loaded dendritic cell (TLPLDC) vaccine in preventing recurrence in resected stage III/IV melanoma patients (randomized, placebo-controlled Phase IIb trial)	Resected stage III/IV melanoma	Autologous DCs loaded with tumor lysate particles (TLPLDC vaccine)	Vaccine improved 24-month disease-free survival (DFS) in patients completing primary vaccine series (62.9% vs. 34.8%).; No DFS difference in intention-to-treat (ITT) analysis.; Supports further Phase III trial combining TLPLDC with checkpoint inhibitors.
Davar et al. (61); 2024	Evaluate neoadjuvant intratumoral TLR9 agonist vidutolimod plus anti-PD-1 nivolumab in high-risk resectable melanoma	High-risk resectable melanoma	Tumor and peripheral immune cells analyzed, especially CD8+ T cells, plasmacytoid dendritic cells / pDCs, myeloid cells, macrophage-related signature	Vidutolimod + nivolumab produced a 55% major pathologic response in high-risk resectable melanoma.; Response was associated with broad immune activation, including increased CD8+ T cells and pDCs in the tumor microenvironment.; Baseline myeloid gene signatures and gut microbiota composition may help predict response.
Vounckx et al. (62); 2024	Evaluate safety, feasibility, and efficacy of SBRT + pembrolizumab with or without intratumoral avelumab/ipilimumab + myeloid dendritic cells in anti-PD-1-pretreated oligometastatic patients	Anti-PD-1-pretreated oligometastatic patients	Isolated autologous CD1c/BDCA-1+ and CD141/BDCA-3+ myeloid dendritic cells / myDCs	SBRT plus pembrolizumab with intratumoral checkpoint blockade and myDC injection was safe and feasible.; Arm A showed a 20% objective response rate, with 2 partial responses among 10 patients.; The trial failed to meet its primary endpoint, as 1-year PFS remained low.
Bhardwaj et al. (63); 2020	Test whether Flt3 ligand / CDX-301 pre-treatment can expand dendritic cells and enhance immune responses to a DC-targeting anti-DEC-205-NY-ESO-1 vaccine	High-risk melanoma patients	DEC-205+ dendritic cells targeted in vivo; no ex vivo cellular vaccine used	Flt3 L/CDX-301 expanded circulating dendritic cells, including cDC1, cDC2, and pDCs.; Anti-DEC-205-NY-ESO-1 vaccine plus poly-ICLC induced significant NY-ESO-1-specific humoral and T-cell responses.
Carpenter et al. (64); 2023	To evaluate whether TLPLDC and TLPO vaccines could prevent melanoma recurrence in high-risk patients	Clinically disease-free stage III/IV melanoma	TLPLDC: ex vivo matured autologous DCs loaded with yeast cell wall particles containing autologous tumor lysate. TLPO: autologous tumor lysate-loaded yeast particles designed for in vivo DC loading	TLPO and TLPLDC without G-CSF were associated with significantly better DFS and OS compared with placebo/TLPLDC+G-CSF groups.; The addition of G-CSF during DC harvest did not improve vaccine efficacy and was linked to poorer survival outcomes
Slingluff et al. (65); 2003	To compare clinical and immunologic responses to a multipeptide melanoma vaccine given either with GM-CSF/Montanide adjuvant or loaded onto monocyte-derived DCs	Advanced melanoma	Two vaccine approaches: 1) melanoma peptides + tetanus helper peptide with GM-CSF and Montanide ISA-51, 2) peptides pulsed on monocyte-derived dendritic cells	The GM-CSF/Montanide peptide vaccine produced stronger melanoma-specific T-cell responses than the DC-pulsed peptide vaccine.; Clinical tumor regression occurred in a small number of patients, mainly in the GM-CSF/adjuvant group.
Saberian et al. (66); 2021	To determine whether adding MART-1 peptide-pulsed DCs to adoptive TIL therapy improves persistence of MART-1-specific T cells and clinical responses	Advanced stage IV melanoma	Tumor-infiltrating lymphocytes / TILs, especially MART-1-specific CD8+ T cells; plus monocyte-derived DCs pulsed with MART-1 peptide	MART-1-specific TILs persisted well after infusion in both treatment arms.; Adding MART-1-pulsed DCs did not significantly improve TIL persistence compared with TIL alone
Storkus et al. (67); 2021	To evaluate the safety and immunologic/clinical activity of a type-1-polarized DC vaccine targeting tumor blood vessel antigens/TBVA combined with dasatinib in HLA-A2+ patients with advanced melanoma	Advanced melanoma: cutaneous	Monocyte-derived type-1-polarized dendritic cells/DC1 loaded with HLA-A2 peptides from TBVA: DLK1, EphA2, HBB, NRP1, RGS5, TEM1; combined with dasatinib	The vaccine induced specific CD8+ T-cell responses against tumor blood vessel antigens in 6/13 evaluable patients.; Responding tumors showed signs of stronger immune activation, including TCR convergence, inflammatory immune infiltration, and formation of tertiary lymphoid structures/TLS.
Jansen et al. (68); 2020	To evaluate the safety and activity of adjuvant TriMixDC-MEL compared with standard follow-up in melanoma patients	Stage III/IV melanoma	Autologous monocyte-derived dendritic cells co-electroporated with mRNA encoding CD40 L, CD70, caTLR4, and melanoma-associated antigens; vaccine known as TriMixDC-MEL	TriMixDC-MEL as adjuvant therapy was safe and tolerable, with only transient local reactions, flu-like symptoms, and chills.; Gene expression profiling suggested four possible predictive biomarkers: STAT2, TPSAB1, CD9, CSF2.

Authors (y)	Main Objective	Stage of disease	Cell type used	conclusion
Chick et al. (69); 2021	To evaluate efficacy of TLPLDC vaccine versus placebo in subgroup analyses of a randomized, blinded phase IIb trial, especially in patients with resected stage III/IV melanoma and possible interaction with checkpoint inhibitors	Resected stage III/IV melanoma, patients rendered disease-free by surgery	TLPLDC vaccine: tumor lysate, particle-loaded, dendritic cell vaccine; a cell-based autologous vaccine strategy	TLPLDC vaccine was safe in resected stage III/IV melanoma patients.; DFS benefit was mainly seen in patients who completed the full vaccine series, especially resected stage IV patients.; Results support phase III testing of TLPLDC with checkpoint inhibitors.
Dillman et al. (70); 2018	To compare autologous tumor cell vaccine / TCV with autologous dendritic cell vaccine / DCV loaded with autologous tumor-associated antigens in metastatic melanoma	Metastatic melanoma	Autologous dendritic cells loaded ex vivo with autologous tumor-associated antigens; compared with autologous tumor cell vaccine	DCV improved overall survival compared with TCV in metastatic melanoma.; Median OS was 43.4 months with DCV vs 20.5 months with TCV.; DCV had minimal toxicity, and DTH reactions did not predict survival benefit.
Ribas et al. (71); 2010	To evaluate the efficacy and antitumor activity of IDD-3 dendritic cell vaccine in favorable-prognosis metastatic melanoma	Limited metastatic melanoma involving skin/subcutaneous tissue/lung; stage IIIc, M1a, M1b	IDD-3: autologous monocyte-derived mature DCs, pulsed with lysates from three allogeneic melanoma cell lines	IDD-3 induced strong immune activation against melanoma antigens.; Antitumor activity was observed, with 1 CR, 2 PR, and tumor growth control rate of 27%.; Toxicity was minimal, supporting further evaluation of mature DC vaccines.
Ellebaek et al. (72); 2012	To evaluate whether adding metronomic cyclophosphamide and celecoxib to a DC vaccine can reduce immunosuppression and improve efficacy	Progressive metastatic melanoma	Autologous DC vaccine pulsed with survivin, hTERT, and p53 peptides in HLA-$A2^+$ patients or tumor lysate in HLA-$A2^-$ patients; combined with IL-2, cyclophosphamide, and celecoxib	Stable disease was observed in 57% of patients, with prolonged SD in some cases.; Immune responses increased after vaccination, but regulatory T cells did not decrease.
van den Hout et al. (73); 2016	To evaluate whether local low-dose CpG-B ± GM-CSF can strengthen immune defenses in the sentinel lymph node, SLN, before SLN excision	Clinical stage I-II melanoma; pre-surgical	DC-targeting immune adjuvant approach: intradermal CpG-B alone or combined with GM-CSF around the melanoma excision site	Low-dose CpG ± GM activated antitumor immunity in the sentinel lymph node, increasing melanoma-specific CD8 T cells.; Treatment also increased Treg activity (FoxP3↑, CTLA-4↑, IL-10↑), partially counterbalancing the immune boost.; SLN metastases were reduced in CpG and CpG+GM groups compared to saline.
Butterfield et al. (74); 2017	to evaluate adjuvant GM-CSF and/or multiepitope melanoma peptide vaccine versus placebo	Completely resected high-risk stage III/IV melanoma	Multiepitope melanoma peptide vaccine: Tyrosinase, gp100, MART-1 peptides in montanide ± GM-CSF as DC-stimulating adjuvant	No significant RFS or OS improvement was observed with peptide vaccine or GM-CSF versus placebo.; Vaccination increased peptide-specific $CD8^+$ T-cell responses compared with no vaccine.; Anti-GM-CSF neutralizing antibodies correlated with improved RFS and OS.
Dillman et al. (75); 2012	To compare two patient-specific immunotherapy products: autologous tumor cell vaccine vs autologous DC vaccine loaded with tumor antigens	Metastatic melanoma	Autologous DC vaccine loaded with antigens from autologous melanoma cells vs irradiated autologous proliferating tumor cell vaccine; both with GM-CSF	DC vaccine improved survival compared with tumor cell vaccine.; Median survival was not reached in the DC arm vs 15.9 months in the tumor cell vaccine arm.; Treatment was well tolerated, supporting DC vaccine as a consolidation immunotherapy.
Schadendorf et al. (76); 2006	To compare autologous peptide-loaded DC vaccination with standard dacarbazine, DTIC, chemotherapy	Stage IV melanoma	Autologous dendritic cell vaccine loaded with MHC class I and II-restricted peptides	DC vaccination was not superior to DTIC chemotherapy in stage IV melanoma.; Objective response was low in both groups: DC 3.8% vs DTIC 5.5%.; Better survival in the DC arm was associated with Karnofsky = 100 and HLA-$A2^+$/HLA-$B44^-$ haplotype.
Bloemendal et al. (77); 2021	To evaluate immunological responses to adjuvant vaccination with naturally occurring dendritic cell subsets in melanoma	Completely resected stage III melanoma	Naturally occurring DC subsets: CD1c+ myeloid dendritic cells / cDC2s, plasmacytoid dendritic cells / pDCs, or their combination	Natural DC vaccine production was feasible for all patients, with vaccines meeting release criteria.; Vaccination induced strong immunological responses: antigen-specific CD8+ T cells were detected in 80% of skin test-derived T cells and 55% of peripheral blood samples.; The treatment was safe, causing only grade 1 - 2 adverse events, mainly fatigue.
Charles et al. (78); 2020	To evaluate the safety, tolerability, and immunogenicity of an allogeneic plasmacytoid dendritic cell line-based melanoma vaccine, and explore its potential combination with immune checkpoint blockade	Metastatic stage IV melanoma	Allogeneic irradiated plasmacytoid dendritic cell line / PDC line, loaded with 4 melanoma antigens; circulating anti-tumor specific T lymphocytes analyzed	The allogeneic PDC line-based vaccine was safe and well tolerated, with no serious vaccine-induced adverse events.; It induced immune activation in some patients, including increased circulating anti-tumor specific T cells and a shift from naïve to memory phenotype.; Preliminary clinical activity was observed, including 4 stable diseases by IrRC, vitiligoid lesions, and survival of 4 patients at week 48; combination with anti-PD-1 was supported by in vitro synergy.
Adams et al. (79); 2023	To compare clinical outcomes and RNA gene-expression profiles of TLPLDC vaccine according to dendritic cell harvest method, with or without G-CSF pretreatment	Resected stage III/IV melanoma	Autologous dendritic cells loaded with autologous tumor lysate packaged in yeast cell wall particles / YCWPs; DCs harvested either by direct blood draw or after G-CSF pretreatment; RNA-seq performed on TLPLDC vs TLPLDC+G vaccines	TLPLDC vaccine without G-CSF improved outcomes, with better 36-month DFS and OS than TLPLDC+G or placebo.; G-CSF pretreatment appeared detrimental or non-beneficial, because TLPLDC+G outcomes were similar to placebo.; RNA-seq showed that directly harvested TLPLDC vaccines had upregulated DC maturation genes and downregulated genes linked to DC suppression or immaturity.
De Keersmaecker et al. (80); 2020	To evaluate TriMixDC-MEL IPI-induced tumor-associated antigen-specific T-cell responses in peripheral blood of melanoma patients	Pretreated stage III/IV advanced melanoma	Monocyte-derived dendritic cells electroporated with mRNA encoding CD70, CD40 L, constitutively active TLR4, and melanoma antigens tyrosinase, gp100, MAGE-A3, MAGE-C2; PBMC-derived T-cell responses analyzed	TriMixDC-MEL + ipilimumab elicited specific T-cell responses against melanoma antigens in most evaluable patients; ELISPOT responses were seen in 12/15 patients.; Patients with complete or partial responses had stronger, broader, and more multifunctional T-cell responses than patients with stable/progressive disease.; Polyfunctional and multiantigen CD8+ T-cell responses may be a benchmark for achieving sustained remission in melanoma.
Santos et al. (81); 2020	To investigate immune and molecular features associated with clinical response to DC vaccines expressing three full-length melanoma antigens	Melanoma patients receiving DC vaccination	Melanoma antigen-specific CD8 T cells, dendritic cells expressing three full-length melanoma antigens, lymphocytes, and tumor samples	Antigen expression level in DCs did not significantly affect T-cell or clinical responses.; Better clinical outcomes were associated with low PD-1 expression on melanoma antigen-specific CD8 T cells.; High immune checkpoint gene expression networks, including PD-1 and CTLA-4, correlated with poorer clinical outcomes.
van Decar et al. (82); 2024	To compare TLPO vaccine with TLPLDC vaccine in patients with resected Stage III/IV melanoma, evaluating recurrence and survival outcomes	Resected Stage III/IV melanoma	TLPLDC: ex vivo dendritic cells loaded with autologous tumor lysate particles.; TLPO: yeast cell wall particles loaded with autologous tumor lysate, injected directly for in vivo DC loading	TLPO and TLPLDC showed equivalent clinical outcomes, with no significant difference in DFS or OS between the two vaccine arms.; Both vaccines were well tolerated, with no difference in related adverse events between treatment groups.; Because TLPO avoids ex vivo DC manufacturing and has practical manufacturing advantages, further testing in a Phase III trial is warranted.
Dasyam et al. (83); 2023	To determine whether adding α-galactosylceramide / α-GalCer to autologous NY-ESO-1 long peptide-pulsed DC vaccines improves NY-ESO-1-specific T cell responses compared with peptide-pulsed DC vaccine alone	Fully resected stage II-IV malignant cutaneous melanoma	Autologous monocyte-derived mature dendritic cells loaded with long NY-ESO-1-derived peptides, with or without α-GalCer; analyzed NY-ESO-1-specific T cells, mainly CD4+ T cells, and type 1 NKT cells	The vaccine was well tolerated and induced increases in total T cell responses, predominantly CD4+ T cells.; Adding α-GalCer did not significantly improve NY-ESO-1-specific T cell responses compared with DC vaccine alone.; NKT cell activation by α-GalCer was limited, with no significant increase in circulating NKT cells or cytokine responses in the α-GalCer arm.
Maurer et al. (84); 2020	To profile autologous DC vaccines used in melanoma patients and identify critical molecules/pathways responsible for effective antitumor immune activation	Melanoma cancer	Autologous dendritic cell vaccines, melanoma patient DCs, antigen-specific CD8+ and CD4+ T cells from naïve donors; analyzed ICOSL, NF-κB signaling	Ex vivo maturation-induced checkpoint/costimulatory molecules in DC vaccines correlated with in vivo vaccine activity.; Melanoma patient DCs showed reduced surface ICOSL expression and defective intrinsic canonical NF-κB signaling, which impaired optimal T-cell priming.; Soluble/extracellular ICOSL released from vaccine DCs positively correlated with clinical outcomes, suggesting ICOSL/NF-κB and ADAM10/17-regulated shedding as therapeutic optimization targets.

Table 2. Clinical Trial Outcomes of DC-Based Vaccines in GBM Patients

Authors (y)	Main Objective	Stage of Disease	Cell Type Used	Conclusion
Yao et al. (88); 2018	To evaluate safety and efficacy of a dendritic cell vaccine loaded with glioblastoma stem cell-like (GSC) antigens in GBM patients (double-blind placebo-controlled phase II trial)	GBM (post-surgery; primary or recurrent GBM)	Autologous DCs loaded with GSC antigens	DC vaccination significantly prolonged overall survival after adjustment for molecular factors.; Patients with IDH1WT / TERT-mutant tumors showed improved OS and PFS with increased IFN-γ and CCL22 levels.; Low B7-H4 expression identified patients more likely to benefit from DC vaccine therapy.
S Vleeschouwer et al. (89); 2008	To investigate feasibility, safety, and therapeutic impact of adjuvant vaccination with autologous mature DCs loaded with autologous tumor lysate in relapsed GBM	Relapsed glioblastoma multiforme (WHO grade IV)	Autologous mature DCs loaded with autologous tumor lysate	DC vaccination was feasible and generally safe, with evidence of some long-term survival.; Faster vaccination schedules showed a trend toward improved progression-free survival.; Better outcomes were associated with younger age and especially minimal residual disease/total resection at vaccination start.
Akiyama et al. (90); 2012	To evaluate safety, feasibility, and immunological/clinical effects of α-type-1 polarized dendritic cell (DC1) immunotherapy in recurrent high-grade glioma patients (HLA-A2/A24)	Recurrent high-grade gliomas (including GBM)	Autologous monocyte-derived α-type-1 polarized DCs pulsed with HLA-A2/A24-restricted synthetic peptides	DC vaccine induced peptide-specific immune responses in majority of patients.; Clinical benefit was limited, but one patient receiving multiple vaccinations showed prolonged recurrence-free survival.
Vik-Mo et al. (91); 2013	To evaluate the feasibility, safety, immunogenicity, and potential clinical benefit of a DC vaccine targeting glioblastoma cancer stem cells (CSCs)	Glioblastoma after surgery and standard post-operative radio-chemotherapy	Autologous monocyte-derived DCs transfected with amplified mRNA from autologous glioblastoma cancer stem cells (tumorspheres)	CSC-targeted DC vaccination induced immune responses in all treated patients.; Vaccinated patients showed markedly longer progression-free survival than matched controls, suggesting potential clinical benefit.
Sakai et al. (92); 2015	To evaluate the safety, feasibility, and immune responses of WT1-pulsed dendritic cell vaccination in patients with relapsed malignant glioma	Relapsed malignant gliomas (6 GBM, others anaplastic gliomas)	Autologous dendritic cells pulsed with WT1 peptide and/or autologous tumor lysate, administered with OK-432 adjuvant	WT1-pulsed DC vaccination was safe and feasible in relapsed malignant glioma patients.; Vaccine induced WT1-specific CTL responses and positive skin reactions in most patients.; Disease stabilization observed in several patients, with tumor shrinkage and neurological improvement in some cases.
Ardon et al. (93); 2012	To evaluate feasibility, safety, and clinical efficacy of integrating dendritic cell vaccination into standard postoperative radiochemotherapy in newly diagnosed GBM	Newly diagnosed glioblastoma	Autologous DC loaded with autologous tumor antigens (tumor lysate-based DC vaccine)	Integration of DC vaccination with standard radiochemotherapy was feasible and safe.; Promising survival outcomes were observed; Better outcomes were associated with favorable prognostic factors such as lower RPA class and MGMT promoter methylation.
Erhart et al. (94); 2018	To investigate immune factors associated with outcome and the immunological effects of Audencel in GBM patients treated in a phase II trial	GBM	Audencel: autologous dendritic cells loaded with autologous whole tumor lysate and matured in vitro with danger signals	Audencel did not improve progression-free or overall survival and showed no clinical efficacy in the phase II trial.; *Despite* lack of clinical benefit, Audencel induced measurable immune activation, including Th1-related responses (e.g., IFN-γ, IL-2, T-bet).; Better survival was associated with favorable pre-existing and post-vaccination immune parameters, suggesting a role for biomarkers and combination strategies.
Sampson et al. (95); 2009	to evaluate the safety and immunogenicity of a DC-based vaccine targeting the tumor-specific EGFRvIII mutation in newly diagnosed GBM	Newly diagnosed GBM after gross-total resection and radiotherapy	Autologous mature DCs pulsed with EGFRvIII-specific peptide conjugated to KLH	EGFRvIII-targeted DC vaccination was safe and feasible in newly diagnosed GBM patients; Most patients developed EGFRvIII-specific immune responses.; Survival outcomes appeared encouraging compared with historical expectations, supporting EGFRvIII as a tumor-specific immunotherapy target.
Chang et al. (96); 2010	To evaluate the clinical and immunological effects of autologous dendritic cell-tumor vaccine therapy in patients with malignant glioma after surgery	Malignant glioma (newly diagnosed and relapsed cases)	Autologous dendritic cells loaded with autologous tumor antigens (DC-tumor vaccine)	DC-tumor vaccination increased tumor-infiltrating $CD8^+$ lymphocytes and showed evidence of tumor shrinkage.; Survival appeared longer compared with historical controls. Treatment was generally safe, with only transient liver enzyme elevations reported.
Ridolfi et al. (97); 2024	To evaluate 3-month PFS and safety of DCvax combined with standard therapy in resected glioblastoma patients	Resected glioblastoma / grade 4	Dendritic cell vaccine using patient-derived tumor material; immune response assessed by DTH skin test to KLH and autologous tumor homogenate	DCvax plus standard RT-TMZ/TMZ therapy was well tolerated in resected GBM patients.; No DCvax-related grade 3 - 4 toxicities were observed in the first 9 evaluable patients.; The trial met its first-step criteria, with median PFS of 12.2 months from surgery, so enrollment continued.
Everson et al. (98); 2024	To evaluate whether adding TLR agonists — poly-ICLC or resiquimod — to ATL-DC vaccination improves immune potency and safety	Newly diagnosed or recurrent WHO grade III-IV malignant gliomas	Autologous tumor lysate-pulsed dendritic cells / ATL-DC; analyzed CD4+ T cells, CD8+ T cells, monocytes, and interferon-response genes	ATL-DC vaccination combined with TLR agonists was safe in malignant glioma patients.; Poly-ICLC enhanced interferon-related immune activation, especially in monocytes and T cells.; Higher interferon-response gene expression correlated with prolonged survival and delayed progression, suggesting a potential blood biomarker.
Bota et al. (99); 2025	To evaluate the feasibility, safety, and clinical outcomes of autologous DC-ATA vaccine added to standard RT/TMZ and adjuvant TMZ	Newly diagnosed glioblastoma	Autologous dendritic cells differentiated from peripheral blood monocytes and loaded with autologous tumor antigens / ATA from short-term autologous tumor cell lines	DC-ATA vaccine was feasible and well tolerated in newly diagnosed GBM patients.; Median PFS was 10.7 months, reported as higher than historical standard-treatment trial medians.; Outcomes worsened after vaccine completion, suggesting longer or extended vaccination may be needed to improve OS.
Mitsuya et al. (100); 2020	To evaluate the therapeutic effect of peptide-cocktail-pulsed α-type-1 DC vaccine combined with standard therapy in newly diagnosed high-grade glioma patients	Newly diagnosed high-grade gliomas	α-type-1 dendritic cells generated from enriched monocytes and pulsed with a cocktail of 5 synthetic peptides; CTL responses analyzed by ELISPOT	α -type-1 DC vaccines produced high levels of IL-12, which may enhance antitumor T-cell immunity.; 10 of 15 evaluable patients developed peptide-specific CTL responses by ELISPOT.; After 6 years, 5 patients were still alive and 2 were relapse-free, suggesting a potential survival benefit.
Liau et al. (101); 2018	To evaluate whether adding DCVax-L, an autologous tumor lysate-pulsed dendritic cell vaccine, to standard therapy improves outcomes in glioblastoma	Newly diagnosed glioblastoma	Autologous dendritic cells pulsed with autologous tumor lysate; vaccine: DCVax-L	DCVax-L was feasible and safe when added to standard surgery, radiotherapy, and temozolomide in newly diagnosed GBM.; Median OS in the ITT population was 23.1 months, and patients with MGMT promoter methylation had longer survival: 34.7 months.; The study showed an extended-survivor population, but interpretation is complicated because nearly 90% of patients eventually received DCVax-L due to crossover.
Bota et al. (102); 2022	To evaluate manufacturing success, safety, and survival outcomes of AV-GBM-1, an autologous DC vaccine loaded with irradiated autologous tumor-initiating cell lysate	Newly diagnosed GBM	Autologous dendritic cells incubated with lysate of irradiated autologous Tumor-Initiating Cells / TICs; vaccine admixed with GM-CSF before subcutaneous injection	AV-GBM-1 manufacturing was highly successful, with 97% success for both TIC production and monocyte collection, and vaccine produced for 63/63 patients.; The vaccine was generally well tolerated, with mainly injection-site reactions and flu-like symptoms attributed to treatment.; mPFS was encouraging at 10.4 months, but mOS was 16.0 months, so no clear overall survival improvement was shown.
Batich et al. (103); 2020	To evaluate long-term clinical outcomes and vaccine migration across sequential clinical trials using CMV-specific DC vaccines in patients with newly diagnosed GBM	Newly diagnosed glioblastoma	Autologous dendritic cells targeting cytomegalovirus / CMV antigens, with assessment of DC vaccine migration to draining lymph nodes	CMV-specific DC vaccines were associated with exceptional long-term survival in a subset of newly diagnosed GBM patients.; Across sequential trials, nearly one third of the vaccinated population remained without recurrence or survived long-term, including 5-year survival rates around 36% in one study.; Enhanced DC migration to draining lymph nodes was observed in a two-arm trial and reproduced in a larger confirmatory study, suggesting a potentially important mechanism for vaccine efficacy.
Wen et al. (104); 2019	To evaluate efficacy, safety, quality of life, and immune response of ICT-107 in newly diagnosed GBM	Newly diagnosed glioblastoma (HLA-A1+ and/or HLA-A2+ patients)	Autologous dendritic cells pulsed with six synthetic peptide epitopes targeting MAGE-1, HER-2, AIM-2, TRP-2, gp100, and IL13Rα2; control arm used unpulsed DC	ICT-107 was safe and well tolerated, with no meaningful difference in adverse events compared with unpulsed DC control.; In the ITT population, PFS improved significantly by 2.2 months, but OS improvement of 2.0 months was not statistically significant.; HLA-A2 patients showed stronger immune responses and greater clinical benefit, suggesting that HLA restriction and antigen presentation strongly influenced vaccine activity.
Inogés et al. (105); 2017	To evaluate feasibility, safety, immune response, PFS, and OS after adding tumor lysate-pulsed autologous DC vaccination to maximal safe resection plus radiotherapy and temozolomide	Newly diagnosed GBM	Autologous dendritic cells generated from peripheral blood monocytes and pulsed with autologous whole tumor lysate	Tumor lysate-pulsed autologous DC vaccination was feasible and safe, with no severe adverse effects related to immunotherapy.; Survival outcomes were encouraging: median PFS = 12.7 months and median OS = 23.4 months.; A tumor-specific immune response after vaccination was detected in 11/27 patients, but this immune response did not correlate with survival.
Cho et al. (106); 2012	To evaluate the effectiveness and safety of adjuvant autologous dendritic cell vaccine immunotherapy in patients with newly diagnosed GBM	Newly diagnosed GBM	Autologous dendritic cell vaccine, described as a whole-cell lysate DC vaccine; 10 vaccine inoculations over 6 months	Adjuvant autologous DC vaccination significantly improved overall survival, with median OS of 31.9 months versus 15.0 months in the control group.; 2-year and 3-year survival rates were significantly higher in the vaccine group, while the 1-year survival difference was not significant.; PFS was only slightly improved in the vaccine group, 8.5 vs 8.0 months, and this difference was not statistically significant.
Hu et al. (107); 2022	To assess the safety and tolerability of an autologous dendritic cell (DC) vaccine in patients with GBM.	Newly diagnosed GBM and recurrent GBM cohorts	Autologous dendritic cells pulsed with lysate derived from an allogeneic GBM stem-like cell line	The autologous DC vaccine was found to be safe and well-tolerated in both newly diagnosed and recurrent GBM patient cohorts.; For newly diagnosed patients, the results were encouraging, with a median PFS of 8.75 months and a median overall survival of 20.36 months.; A subset of participants exhibited a measurable cytotoxic T-cell response, supporting the potential efficacy of immunotherapy as a treatment strategy for this aggressive malignancy.
Liau et al. (108); 2005	o evaluate the feasibility, safety, and ability of autologous dendritic cell vaccination to induce systemic and intracranial T-cell responses in patients with glioblastoma multiforme.	Patients with histologically confirmed glioblastoma multiforme	Autologous dendritic cells pulsed with acid-eluted autologous tumor peptides	The vaccine induced measurable immune activity: 6 patients developed systemic antitumor CTL responses, and increased intratumoral cytotoxic T-cell infiltration was seen in some reoperated patients.; Clinical benefit seemed more likely in patients with less bulky or non-actively progressing tumors and tumors with low TGF-β2 expression, suggesting that tumor microenvironment factors strongly influence vaccine response.
Jan et al. (109); 2018	To retrospectively evaluate clinical and immunological factors affecting outcomes in de novo GBM patients treated with autologous dendritic cell/tumor antigen vaccine therapy.	Newly diagnosed / de novo GBM	Autologous dendritic cells loaded with tumor antigens; described as autologous dendritic cell/tumor antigen vaccine, or ADCTA	Better outcomes were associated with younger age, gross total resection, and receiving CCRT with temozolomide.; A lower $PD\text{-}1^+/CD8^+$ ratio in tumor-infiltrating lymphocytes predicted longer OS and PFS.; A lower $PD\text{-}1^+/CD8^+$ ratio in PBMCs also predicted better survival and correlated with the tumor immune profile.
Batich et al. (110); 2017	To evaluate pp65-specific cellular immune responses after dose-intensified temozolomide with pp65-targeted dendritic cell vaccination,			

Authors (y)	Main Objective	Stage of Disease	Cell Type Used	Conclusion
	and to assess effects on long-term PFS and OS in GBM patients	Newly diagnosed glioblastoma	Autologous dendritic cells pulsed with cytomegalovirus pp65 LAMP mRNA, given with GM-CSF	pp65-specific immune responses significantly increased after DI-TMZ plus three doses of pp65-DC vaccine.; Patients showed prolonged survival, with median PFS of 25.3 months and median OS of 41.1 months.; *Despite* increased regulatory T cells/Tregs after DI-TMZ, long-term PFS and OS were still observed.
Phuphanich et al. (111); 2013	To evaluate the safety and immune responses induced by ICT-107, an autologous dendritic cell vaccine pulsed with class I peptides from glioma-associated antigens	Mainly newly diagnosed GBM	Autologous dendritic cells pulsed with class I TAA peptides: HER2, TRP-2, gp100, MAGE-1, IL13Rα2, and AIM-2	ICT-107 was associated with immune responses in a subset of newly diagnosed GBM patients, with 33% immune responders among evaluable patients.; Higher pre-vaccine expression of several target antigens, especially MAGE-1 and AIM-2, correlated with longer PFS and OS.; Median survival outcomes in newly diagnosed GBM were encouraging: median PFS was 16.9 months and median OS was 38.4 months.
Prins et al. (112); 2011	To assess the feasibility, safety, and toxicity of autologous tumor lysate-pulsed dendritic cell vaccination combined with TLR agonists, and to correlate clinical/immune responses with tumor gene expression profiles	Newly diagnosed and recurrent glioblastoma	Autologous dendritic cells pulsed with autologous glioma tumor lysate, followed by booster vaccination with TLR agonist adjuvants: imiquimod or poly-ICLC	Median overall survival was 31.4 months, with 1-, 2-, and 3-year survival rates of 91%, 55%, and 47%, respectively.; Patients with mesenchymal gene expression signatures appeared more responsive to DC vaccination and had more $CD3^+/CD8^+$ tumor-infiltrating lymphocytes

Table 3. Clinical Trial Outcomes of DC-Based Vaccines in Prostate Cancer

Authors (y)	Main Objective	Stage of Disease	Cell Type Used	Conclusion
Xi et al. (116); 2002	To evaluate safety, feasibility, and efficacy of DC vaccine loaded with rPSMA and rSurvivin peptides versus Docetaxel in hormone-refractory prostate cancer	Hormone-refractory prostate cancer (HRPC)	Autologous DCs loaded with recombinant PSMA and Survivin peptides Autologous DCs loaded with recombinant PSMA and Survivin peptides	DC vaccination induced immune responses (DTH) in all patients.; The DC arm demonstrated a higher objective response rate (ORR 72.7%) compared to the chemotherapy arm.; Disease stabilization and partial remissions were achieved, suggesting rPSMA/Survivin-DC vaccines are a safe and potent alternative to standard chemotherapy.
Thomas Kaskel et al. (117); 2006	To evaluate feasibility, safety, and induction of antigen-specific immunity using PSCA and PSA peptide-pulsed DCs	Hormone- and chemotherapy-refractory prostate cancer	Autologous mature DCs pulsed with PSCA and PSA HLA-A2 binding peptides	DC vaccination targeting PSCA/PSA is safe and feasible in refractory patients.; Immune responses (DTH/tetramer) were linked to superior clinical outcomes.; Vaccine efficacy appears dependent on the patient's baseline immune competence.
Castiello et al. (118); 2017	To identify DC molecular markers correlating with clinical and immunologic responses in TARP-peptide vaccination	Prostate carcinoma	Peptide-pulsed DCs (TARP)	DCs with a "less tolerogenic" gene signature are significantly more potent in inducing immune responses.; Specific markers (low CD14, IL-10, MCP-1 and high MDC) were identified as predictors of vaccine potency.; In-depth molecular characterization of DC products is critical to overcome the clinical efficacy hurdle in cell-based therapies.
Sonpavde et al. (119); 2017	To evaluate safety and activity of BPX101 (CD40-modified APC vaccine) activated in vivo by Rimiducid	Metastatic castration-resistant prostate cancer (mCRPC)	Ad5f35-transduced autologous APCs expressing inducible CD40 (BPX101)	BPX101 allows for controlled, lymphoid-localized DC activation using a bioinert drug.; The platform showed promising clinical signals, including PSA declines and objective tumor regressions.; The strategy of combining antigen-targeting with inducible co-stimulation represents a robust, next-generation immunotherapy platform.
Frank et al. (120); 2010	To evaluate safety and immunogenicity of an apoptotic tumor-DC vaccine modeled on PND immune responses	Prostate cancer	Autologous DCs pulsed with apoptotic allogeneic prostate tumor cells	The vaccine successfully induced both CD4+ and CD8+ T-cell proliferation without affecting regulatory T cells (Tregs).; It demonstrated significant clinical impact by slowing PSA velocity and doubling PSA doubling time.; Using apoptotic tumor cells is a potent strategy to harness natural anti-tumor immunity.
Pandha et al. (121); 2004	To assess feasibility, toxicity, and immunogenicity of DC vaccine in advanced urological cancers	Hormone-refractory prostate cancer and metastatic renal cell carcinoma	Allogeneic tumor lysate-pulsed DCs (adjuvanted with KLH)	Cryopreservation of DC aliquots ensures consistent quality control and facilitates repeated administration.; The vaccine successfully induced both humoral and cellular (Th1/IFN-γ) immune responses.; Clinical benefit was observed in a subset of patients, including PSA stabilization/reduction and disease stabilization in renal cancer.
Waeckerle-Men et al. (122); 2006	To evaluate the immunostimulatory capacity of autologous dendritic cells pulsed with multiple T-cell epitopes derived from four prostate-specific antigens in patients with advanced prostate cancer.	Advanced hormone-refractory prostate cancer	Autologous dendritic cells loaded with peptide epitopes from PSCA, PAP, PSMA, and PSA	The vaccine induced significant cytotoxic T-cell responses against all tested prostate-specific antigens.; Long-term vaccination with booster injections was associated with an increased PSA doubling time.
Rodríguez-Ruiz et al. (123); 2018	To evaluate the safety, immune activity, and preliminary clinical efficacy of a combination radio-immunotherapy strategy using tumor-lysate-loaded dendritic cell vaccination, intratumoral Hiltonol, cyclophosphamide, and SABR in advanced cancer patients.	Advanced cancer patients; included a heavily pretreated castration-resistant prostate cancer patient	Monocyte-derived dendritic cells loaded with autologous tumor lysate and matured with poly-ICLC, TNF-α, and IFN-α; combined with intratumoral Hiltonol and SABR	The combination treatment was safe and well tolerated.; No objective responses were observed, but stable disease occurred in 9 patients, especially in the radiotherapy cohort.; The treatment induced immune-associated activity and showed signs of preliminary clinical efficacy, including an abscopal response in one prostate cancer patient.
Xi et al. (116); 2015	To evaluate the safety, feasibility, clinical response, and immunological effects of a dendritic cell vaccine loaded with recombinant PSMA and Survivin peptides in patients with hormone-refractory prostate cancer (HRPC).	HRPC	Autologous dendritic cells loaded with recombinant PSMA and Survivin peptides; administered subcutaneously	DC vaccination was safe and well tolerated, with no grade 2 toxicity reported.; The vaccine induced cellular immune responses and delayed-type hypersensitivity in all patients.
Thomsen et al. (124); 2023	To evaluate the safety, tolerability, immune effects, and preliminary clinical activity of combining prostate cryoablation with intratumoral autologous immature dendritic cells, with or without checkpoint inhibitors, in metastatic castration-resistant prostate cancer (mCRPC).	mCRPC	Prostate cryoablation + intratumoral autologous immature dendritic cells; in the second part, combined with checkpoint inhibitors (ipilimumab or pembrolizumab)	The combination was safe and well tolerated, with no dose-limiting toxicities and no adverse events grade 3.; Signs of antitumor immune activity were observed, including altered T-cell receptor repertoires.; About 33% of patients showed durable clinical benefit (>46 weeks), with a median overall survival of 40.7 months.; These findings support further phase II evaluation with biomarker-focused design.
Tryggestad et al. (125); 2022	To evaluate whether a personalized dendritic cell vaccine could reduce the risk of biochemical relapse (BCR) after surgery in patients with high-risk prostate cancer	High-risk prostate cancer after robot-assisted laparoscopic prostatectomy (RALP),	Personalized dendritic cell (DC) vaccine	11 of 20 patients remained BCR-free after long-term follow-up.; Vaccine-induced immune responses were associated with lower BCR risk, especially in high-risk subgroups such as EPE and ISUP grade 5 disease.
Vonderheide et al. (126); 2004	To evaluate the safety, immunologic feasibility, and clinical impact of targeting human telomerase reverse transcriptase (hTERT) using a dendritic cell vaccine in advanced cancer patients	Advanced breast or prostate carcinoma; HLA-A2-positive patients	Ex vivo generated autologous dendritic cells pulsed with the HLA-A2-restricted hTERT I540 peptide, presented with keyhole limpet hemocyanin (KLH)	hTERT-specific T-cell responses were induced in 4 of 7 vaccinated patients, confirmed by tetramer, ELISPOT, and cytotoxicity assays.; The vaccine was well tolerated, with no significant toxicity despite hTERT expression in rare normal cells.; Clinical activity was limited but biologically meaningful: one patient showed partial

Authors (y)	Main Objective	Stage of Disease	Cell Type Used	Conclusion
				tumor regression associated with CD8+ tumor-infiltrating lymphocytes.
Kongsted et al. (127); 2017	To investigate whether adding an autologous dendritic cell vaccine (DCvac) to docetaxel induces immune responses and improves clinical outcomes in patients with metastatic castration-resistant prostate cancer	mCRPC	Autologous monocyte-derived dendritic cell vaccine (DCvac)	The addition of DCvac to docetaxel was safe, with vaccine-related toxicity mainly limited to local injection-site reactions.; Immune responses were induced in a substantial proportion of patients, with about 50% showing TAA-specific ELISpot responses and 78% showing vaccine-specific DTH responses.; *Despite* immunologic activity, no significant improvement was seen in PSA response, progression-free survival, or disease-specific survival compared with docetaxel alone.
Fuessel et al. (128); 2006	To evaluate the safety, feasibility, and immunologic/clinical activity of a dendritic cell vaccine loaded with a peptide cocktail derived from multiple prostate cancer-associated antigens	HRPC	Autologous dendritic cells loaded with an HLA-A*0201-restricted peptide cocktail derived from PSA, PSMA, survivin, prostein, and trp-p8	The vaccine was safe and feasible, with only local skin reactions reported.; Limited but encouraging clinical activity was observed: one patient achieved a partial PSA response and three others had stable PSA values or slower PSA increase. Antigen-specific CD8+ T-cell responses were detected in some clinical responders, particularly against prostein, survivin, and PSMA.
Westdorp et al. (129); 2019	To investigate the immunological response and clinical outcome of vaccination with blood-derived dendritic cell subsets in patients with castration-resistant prostate cancer	Chemo-naive castration-resistant prostate cancer (CRPC)	Blood-derived mature CD1c+ myeloid dendritic cells (mDCs), plasmacytoid dendritic cells (pDCs), or a combination of both, stimulated with protamine/mRNA and loaded with NY-ESO-1, MAGE-C2, and MUC1	Functional antigen-specific T cells were induced, particularly in delayed-type hypersensitivity skin-test biopsies rather than only peripheral blood.; Patients who developed functional antigen-specific T cells had better radiologic outcomes, with longer median rPFS compared with those without such T-cell responses.
Perambakam et al. (130); 2006	To determine whether the HLA-A2-restricted PSA-derived peptide (PSA146 - 154) can induce specific anti-tumor T-cell immunity in prostate cancer patients	Locally advanced or metastatic prostate cancer	Vaccination with PSA146 - 154 peptide + GM-CSF by intradermal injection, or autologous dendritic cells pulsed with PSA146 - 154 peptide by intravenous administration	About 50% of patients developed positive DTH responses, indicating induction of antigen-specific cellular immunity.; T cells recovered from DTH sites showed PSA-specific cytokine responses and, in some patients, cytolytic CD8+ activity.; The immune response was predominantly type-1 biased (especially IFN-γ and TNF-α), suggesting biologically meaningful T-cell activation.; The study supports immunogenicity, but does not establish strong clinical benefit such as survival improvement.
Fucikova et al. (131); 2018	To evaluate the safety and biological activity of DC-based immunotherapy in prostate cancer patients with rising PSA, a setting of presumed low tumor burden	Biochemical recurrence / rising PSA after prior treatment	Autologous dendritic cells pulsed with killed LNCaP cells (DCVAC/PCa)	PSA doubling time (PSADT) significantly increased after immunotherapy, suggesting slower biochemical progression.; PSA-reactive T lymphocytes increased early during treatment and remained stable.; The study supports immunogenicity and possible slowing of biochemical relapse, but definitive clinical benefit (e.g. metastasis-free survival or OS) was not proven.
Scheid et al. (132); 2016	Evaluate the safety, immunogenicity, and biological activity of a Tn-MUC1 glycopeptide-loaded dendritic cell (DC) vaccine, supported by preclinical rhesus macaque studies.	Nonmetastatic castrate-resistant prostate cancer (nmCRPC)	Autologous dendritic cells loaded with Tn-MUC1 glycopeptide (tumor-associated hypoglycosylated MUC1 carrying Tn antigen) plus KLH control antigen.	Preclinical studies showed Tn-MUC1 glycopeptide induced much stronger humoral and cellular immune responses than unglycosylated MUC1 peptide.; Tn-MUC1-loaded DCs generated significant MUC1-specific CD4+ and/or CD8+ T-cell cytokine responses in patients.; Vaccine was well tolerated with no significant clinical toxicity and demonstrated biological activity through prolonged PSADT.
Prue et al. (133); 2015	To evaluate the safety, feasibility, and immunologic activity of a dendritic cell vaccine using purified CD1c (BDCA-1) blood-derived dendritic cells loaded with prostate cancer-specific peptides	Advanced metastatic, hormone-refractory prostate cancer (HLA-A*0201 positive patients)	Autologous CD1c (BDCA-1) blood-derived dendritic cells (BDC) loaded with tumor-associated peptides (PSA, PAP, PSMA) + influenza control peptide + KLH	The vaccine was safe and well tolerated, with mainly grade 1 - 2 adverse events such as fever, pain, and injection-site reactions.; The study demonstrated the practical feasibility of using naturally circulating CD1c+ dendritic cells as a DC vaccine platform, although clinical efficacy was not established in this Phase I trial.