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Review

Dendritic Cell Therapy in Immuno-Oncology: A Potentially Key Component of Anti-Cancer Immunotherapies

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Simple Summary

The limited efficacy and severe side effects of traditional anti-tumor therapies prompted a paradigm shift in practical oncology in the past decade. This includes innovative approaches like cancer immunotherapy that aims to exploit the anti-cancer capacity of the innate immune system. Accordingly, numerous new concepts of immune oncology have been developed in recent years, including the use of immune checkpoint inhibitors or genetically engineered T lymphocytes. However, the observed variable clinical effectiveness calls for further developments like those that rely on dendritic cells, master regulators of lymphocyte activation through antigen presentation. Here, we review these efforts, including the ongoing clinical trials and potential future directions of the use of them in clinical practice.

Abstract

Dendritic cells (DCs) are a heterogeneous population known for antigen presentation and immune modulation, playing a key role in priming a T cell response against pathogens and tumor cells. Despite their putative therapeutic value, their scarcity in peripheral blood limited their direct use in therapeutic applications until recently. The discovery that DCs can be generated from circulating monocytes ex vivo, however, gave a boost of extensive research in the use of DCs in clinical applications. Still, despite the numerous clinical trials, the introduction of DCs in the everyday clinical oncology practice is delayed. In this narrative review, we provide an updated summary of the field covering the theoretical and practical aspects of the concept of the use of DCs in adoptive cellular immunotherapy and the completed or ongoing clinical trials for the use of these species in clinical oncology practice. To better understand the current developments of the field, we included those clinical trial reports that published evaluable data to date. Based on our literature survey, DC-based adoptive cellular therapy is a safe therapeutic intervention with valuable clinical potential. Its widespread implementation, however, is likely delayed due to a number of factors that make meaningful evaluation of clinical trial results complicated. These include the great variety of preclinical trial concepts, difficult and heterogenous patient cohorts, and the diversity of intervention techniques applied. Since these factors might hinder the routine implementation of DC-based applications in the more widespread forms of immunotherapy, one of the urgent short-term future directions seems to be the standardization of the DC-based methodologies.



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Keywords: dendritic cells; antigen presentation; cellular adoptive immunotherapy; cancer immunotherapy; clinical trials

1. Introduction

In 2022, cancer was considered to be responsible for one in every six deaths (16.8%) world-wide, representing one of the top three leading causes of premature death in the majority of surveyed countries [1,2]. This accounted for an estimated 20 million new cases and 9.7 million deaths in 2022 [1]. Assuming unchanged cancer rates, a 77% increase in cancer incidence is predicted by 2050, accounting for up to 35 million new cases. This would almost double cancers deaths with the currently available therapeutic tools calling for new approaches.

Indeed, the cellular plasticity and heterogenicity of tumors, in particular the presence of therapy-induced senescence under current therapeutic regimes, makes the efficacy of standard, canonical, not-individualized treatments limited [3,4]. Moreover, canonical therapeutic applications directly deteriorate the endogenous anti-tumor immunity, eliminating a critical factor of natural measures counteracting neoplasms [5]. With our expanding knowledge on genomics, this notion led to a recent paradigm shift from canonical histology-based cancer type-specific modalities to biomarker-centric approaches [6]. The emerging tumor-agnostic philosophy of biomarker-driven approaches in precision medicine attempts to treat patients on the basis of the particular genetic or molecular signatures of their tumor cells, regardless of their histological origin or the anatomical location of the neoplasm [7,8]. Although it also faces challenges due to co-occurring mutations, distinct microenvironments and therapy-induced resistance, this genome-informed and -oriented approach apparently redefines practical oncology, including the rapid implementation of immuno-oncology methodologies [9].

Immuno-oncology is a type of cancer treatment that utilizes, enhances, or modifies a patient's own immune system to attack cancer cells. In contrast to traditional anti-cancer interventions, that rather deplete immunocompetent species, immuno-oncology treatments focus on a patient's immune ecosystem to exploit the endogenous immune cells' capacity to discover and eliminate transformed cells [5,10]. Stimulation of the anti-cancer immune machinery is believed to ensure specificity and immune memory that allows defense against cancer neoantigens even after therapy is discontinued, a critical therapeutic aspect considering the immune system-escaping strategies of cancer cells [4,11].

The first immuno-oncology approaches widely implemented in the clinical practice were centered around immune checkpoint inhibitors that deliberate immune cells paralyzed by cancer species, allowing them to become reactive against neoantigen-harboring cancer cells [11]. While combining immune checkpoint inhibitors with chemotherapy has expanded treatment options for cancers, this approach has shown no clinical benefit in immune desert, also referred to "cold", neoplasms characterized by the lack of reactive lymphocytes, or in patients with dysfunctional or exhausted T cells [11,12]. To address this challenge, professional antigen-presenting cellular elements of the immune system—like the dendritic cells (DC), capable of bridging the innate and adaptive immune systems—have been explored as a promising platform for novel therapeutic interventions.

In this narrative review, we provide an updated summary of the field covering the theoretical and practical aspects of the concept of the use of DCs in adoptive cellular immunotherapy and the completed or ongoing clinical trials that have published evaluable results.

2. Dendritic Cells

2.1. Microscopic Characteristics of Dendritic Cells

Dendritic cells were first described by Steinman and Cohn as a small population of cells morphologically distinct from known lymphoid species and named after their unique stellate shape (Figure 1) [13]. They were found to be most abundant in mice spleen, accommodating for around 1–1.5% of all nucleated cells, though they were also found in Peyer’s patches and lymph nodes [13].

This new class of cells were shown to have large nuclei and mitochondria with a per-nuclear region usually filled with the Golgi apparatus, few small lysosomes with varying contents, and numerous rough and smooth-surfaced vesicles surrounded by a smooth cell surface without any microprojections. The most distinguishing characteristic of dendritic cells was reported to be their relatively electron-lucent ground cytoplasm, which sets them apart from other nucleated leukocytes, especially from lymphocytes (Figure 1) [13].

2.2. Ontogeny of Dendritic Cells

DC development originates in the bone marrow from hematopoietic stem cells [14]. Granulocyte-monocyte-DC progenitors give rise to monocyte/DC progenitors, which have the potential to develop into all DC subsets [14] (Figure 2). Analyses of their molecular makeup revealed that typical DCs show elevated expression of major histocompatibility complex class II molecules and integrin CD11c but do not display the typical surface markers found on B cells, T cells, macrophages, or granulocytes (Figure 1) [15,16]. Further studies revealed that DCs can be divided into functionally different subsets like the CD11c⁺ CD123[−] conventional myeloid and CD11c[−] CD123⁺ plasmacytoid lymphoid DCs [17,18]. When monocyte/DC progenitors differentiate into common DC progenitors, first, they lose their capacity to become monocytes [14]. This species, then, can differentiate into either plasmacytoid DCs or circulating pre-conventional DC progenitors. The latter ones can further differentiate into conventional DCs (cDC) by lineage-determining transcription factor-orchestrated processes [14]. cDC can be further classified into two subsets, conventional type 1 DCs (cDC1) expressing CD141 (BCDA3) and conventional type 2 DCs (cDC2) expressing CD1c (BDCA1) and CD11b (Figure 2) [19–21]. The development of the former one is strictly dependent on the basic leucine zipper ATF-like transcription factor 3 (BATF3), while the development of the latter one is linked to transcription factors Interferon Regulatory Factor 2 and -4 (IRF2 and IRF4) [22–24].

2.3. Antigen Capture and Processing by Dendritic Cells

Physiologically, DCs play the central role in triggering immune reactions via the process called antigen presentation (Figure 3). Differentiated DCs capture, process, and present antigens to T cells [25]. In case of exogenous antigens, this process begins with the internalization of antigens via non-selective macropinocytosis, selective phagocytosis (e.g., of apoptotic bodies or opsonized particles), or receptor-mediated endocytosis (targeting smaller or soluble antigens) [13,26]. The constitutive, non-selective macropinocytosis is mediated by aquaporins like AQP3 and AQP7 that are expressed in immature DCs and ensure the uptake of large quantities of solutes that may contain soluble extracellular antigens [27]. In contrast, selective antigen uptake is mediated by a variety of receptors, including Fc receptors, complement receptors, C-type lectins, and scavenger receptors [26,28–30].

Following antigen internalization, dendritic cells generate macropinosomes, phagosomes, and endosomes. These early endocytic vesicles subsequently fuse with late endosomal compartments containing MHC II molecules, initiating the degradation of internalized proteins [31,32]. Within these vesicles, the chaperone HLA-DM catalyzes the exchange

of the MHC II-associated CLIP fragment for high-affinity antigenic peptides [33]. Once bound, the MHC II-peptide complex is transported to the plasma membrane for antigen presentation [34].

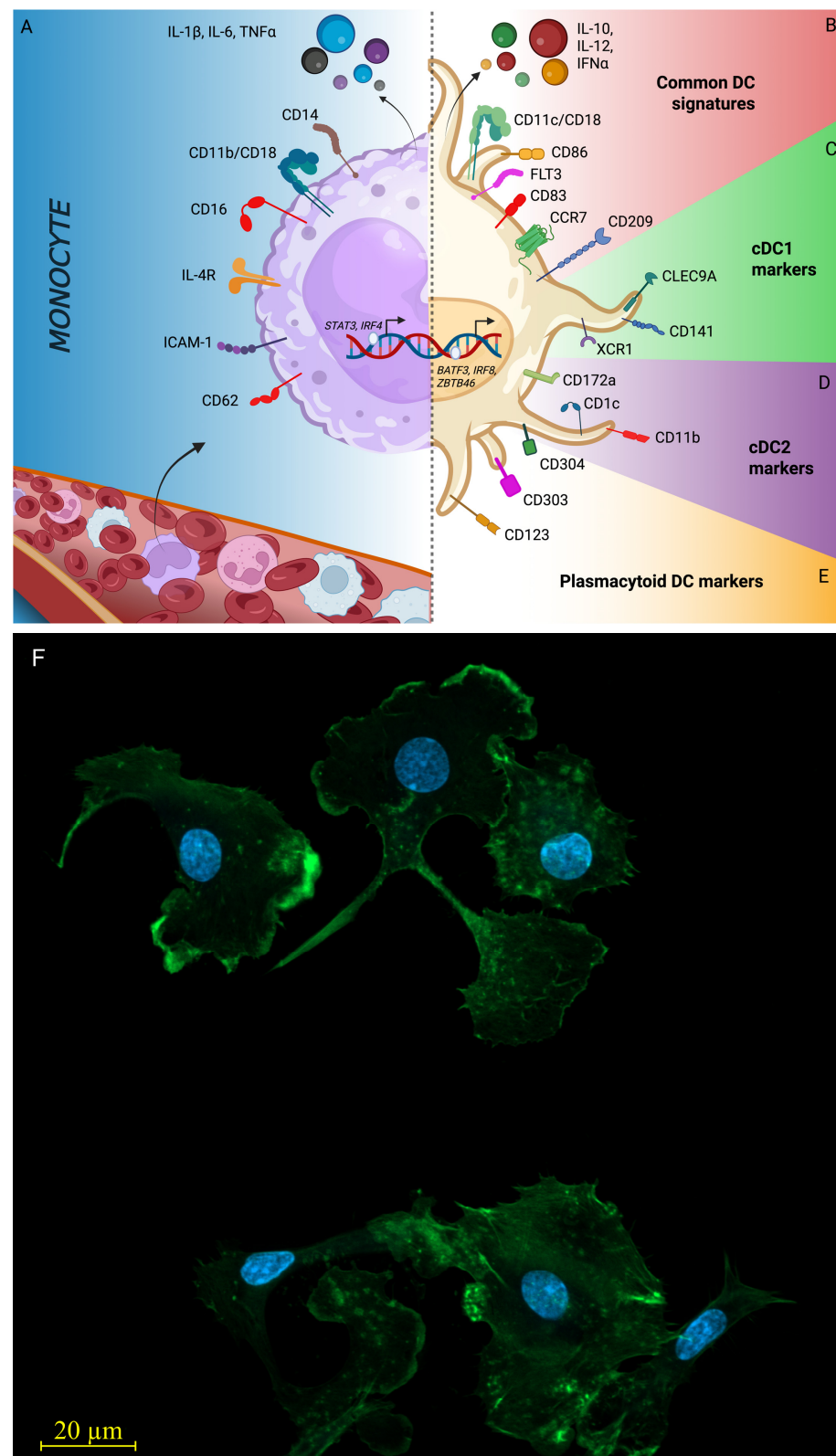


Figure 1. (A) Schematic comparison of the molecular and structural characteristics of dendritic cells and monocytes. Circulating monocytes display high expression of either CD14 or CD16, as well as CD11b, ICAM-1, and CD62L, and are characterized by STAT3 and IRF4-driven gene expression. They primarily secrete pro-inflammatory cytokines like IL-1 β , IL-6, and TNF- α . (B–E) In contrast, dendritic

cells exhibit CD11c/CD18, CD86, FLT3, CD83, CCR7, and CD209 and are transcriptionally marked by BATF3 (Basic Leucine Zipper ATF-like Transcription Factor 3), IRF8 (Interferon Regulatory Factor 8), and ZBTB46 (Zinc Finger and BTB Domain Containing 46). DCs preferentially secrete IL-10, IL-12, and type I interferons (e.g., IFN- α) along with demonstrating enhanced antigen capture and T cell priming functions. Subset-specific regions further delineate DC phenotypes: (C) classical type 1 DCs (cDC1) express CLEC9A, CD141, and XCR1; (D) classical type 2 DCs (cDC2) express CD1c, CD172a (SIRP α), and CD11b; (E) while plasmacytoid DCs (pDCs) express CD123, CD303, and CD304. The figure was created with Biorender.com. (F) Representative image of dendritic cells differentiated from monocytes *in vivo*. Monocytes were isolated from PBMC using CD14-magnetic beads and differentiated into dendritic cells with the addition of GM-CSF and IL-4. Dendritic cells were collected on the 5th day of differentiation and plated on a fibrinogen-coated coverslip. Microfilaments and nuclei were stained with phalloidin-Alexa488 (Molecular Probes, Invitrogen, Cat A12379, Eugene, OR, USA) and Hoechst 33342 (Thermo Fisher Scientific Cat. #62249, Carlsbad, CA, USA), respectively. Confocal microscopy images were collected using an alpha Plan-Apochromat 63x/1.46 Oil Corr M27 objective of a Zeiss LSM800 Axio Observer Z1/7 system (Carl Zeiss AG, Oberkochen, Germany). Courtesy of Szilvia Lukacsi.

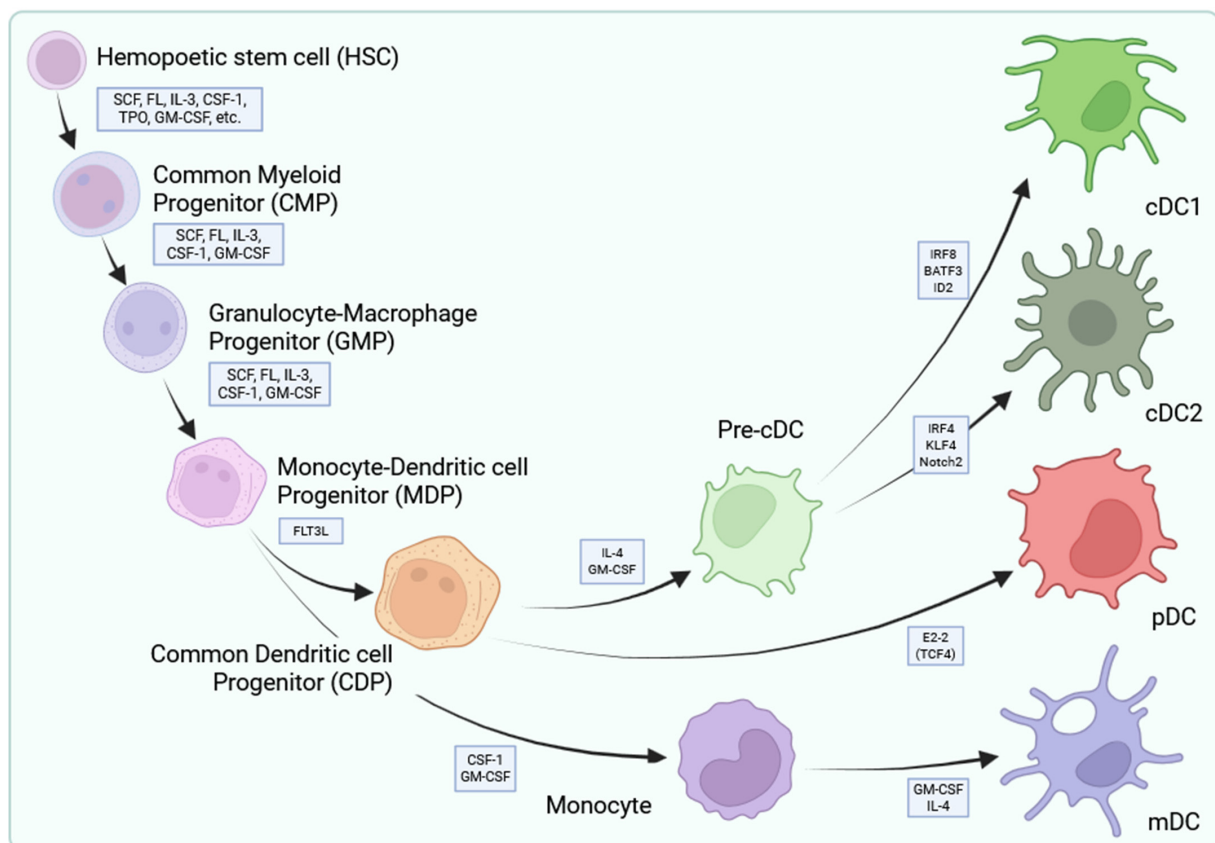


Figure 2. Histological origin of dendritic cells. Hematopoietic stem cells (HSCs) in the bone marrow differentiate into granulocyte-macrophage progenitors (GMPs) via intermediate species termed common myeloid progenitors (CMPs). Under the influence of specific cytokines (SCF, FL, IL-3, CSF-1, GM-CSF), GMPs give rise to monocyte-dendritic cell progenitors (MDPs) from which differentiation can branch into two main lineages: the monocyte lineage, which gives rise to monocyte-derived dendritic cells (mDCs) and macrophages in peripheral tissues via monocytes, and the conventional DC lineage, in which MDPs differentiate into common dendritic cell precursors (CDP). These can directly give rise to plasmacytoid dendritic cells (pDCs) through E2-2 (TCF4)-dependent transcriptional programming or to pre-conventional dendritic cells (pre-cDCs) upon the activity of FLT3L signaling which subsequently differentiate into cDC1 or cDC2 subsets. The figure was created with Biorender.com.

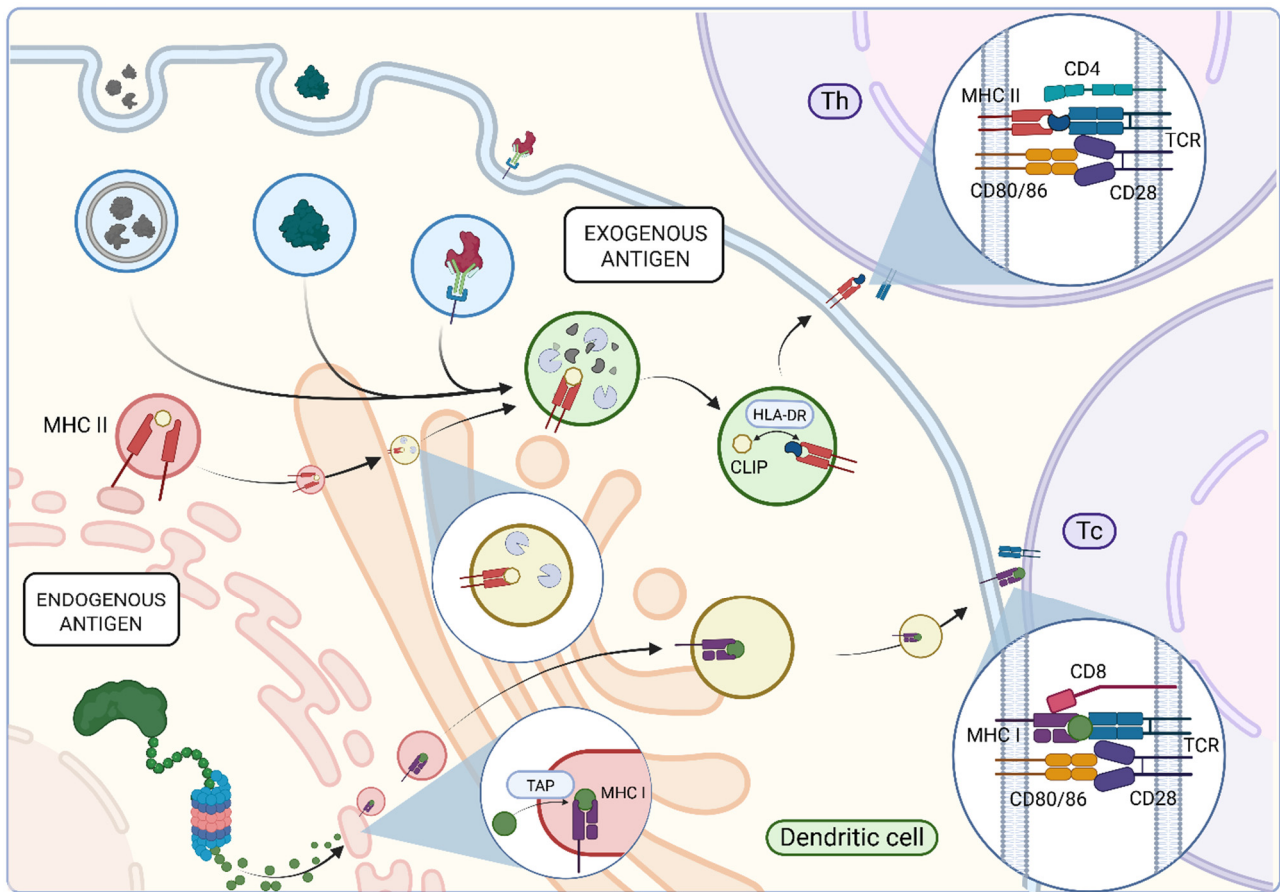


Figure 3. Antigen capture, processing, and presentation by dendritic cells. Dendritic cells have the capacity to present both endo- and exogenous antigens, thereby enabling immune surveillance against extracellular and intracellular factors. During the exogenous antigen presentation, major histocompatibility complex class II (MHC II) molecules are assembled in the endoplasmic reticulum (ER) in association with the invariant chain containing the class II-associated invariant chain peptide (CLIP) and form late endosomes. Dendritic cells can internalize exogenous antigens through selective phagocytosis, macropinocytosis, or receptor-mediated endocytosis. Antigen-transporting primary endosomes fuse with MHC II-marked late endosomes where the proteolytic degradation of the engulfed cargo occurs. Exchange of CLIP for peptides generated from processed antigens is mediated by HLA-DM, resulting in stable MHC II-peptide complexes that are, eventually, delivered to the cell membrane for presentation to CD4⁺ T helper (Th) cells. In the endogenous pathway, in contrast, cytosolic proteins are degraded by the proteasome and the resulting peptides are transported into the ER via transporter associated with antigen processing (TAP) and loaded onto MHC I proteins. The complex, then, is transported to the cell surface to be recognized by CD8⁺ cytotoxic T (Tc) cells. In both cases, effective T cell activation requires additional costimulatory signaling like CD80/86-CD28 connection. The figure was created with Biorender.com.

In case of endogenous proteinaceous antigens, polypeptides undergo degradation via the ubiquitin-proteasome pathway, and the resulting peptide fragments are transported to the endoplasmic reticulum (ER) by the transporter associated with antigen processing (TAP) molecule [35,36]. Peptides of appropriate size, usually 8 to 10 amino acids, and sequence bind to MHC I molecules with the assistance of the peptide-loading complex which includes TAP and the chaperon Tapasin proteins [37]. The MHC I-peptide complex is then transferred by vesicular transport, first, through the Golgi and, then, via secretory vesicles to the plasma membrane (Figure 3) [38].

2.4. Antigen Presentation by Dendritic Cells

Matured, antigen-presenting DCs facilitate T cell activation through multiple signals in the lymph nodes. The MHC II-peptide complex activates CD4⁺ T cells (helper T cells, T_h), while the MHC I-peptide complex activates CD8⁺ T cells (cytotoxic T cells, T_c) through their T cell receptors (TCR) [39,40]. These interactions are further stabilized by CD4 and CD8 co-receptors and additional stimulatory factors like CD80-CD28 engagement [41]. In terms of antigen presentation, dendritic cells have a unique ability to present exogenous antigens on MHC I, a process termed cross-presentation. This process allows DCs to activate CD8⁺ T cells against exogenous antigens like neoantigens of cancer cells by protecting exogenous antigens from immediate degradation. Upon cross-presentation, antigens stored within endosomal compartments are degraded by intra-endosomal proteases or, alternatively, transported to the cytosol and processed by immunoproteasomes [42–45]. From the cytosolic pathway, these peptides are TAP-dependently imported back into endosomal compartments or the ER for loading onto MHC I molecules, after which the peptide-MHC I complex is transferred to the plasma membrane [46,47]. Besides these physical interactions, DC-derived cytokines are also important regulators of the DC-triggered differentiation of T cells into distinct T_h or T_c subtypes (recently reviewed in [48]).

During their lifespan, DCs exist in immature and mature states. In the immature stage, they are scattered through peripheral non-lymphoid tissues and act as the body's first line of defense, constantly monitoring the local environment [49]. They exhibit low expression of MHC I and -II, and the costimulatory molecules CD80, CD83, and CD86 [49]. Being exposed to pathogens, they pick them up and process their antigens to eventually move to lymphoid tissues. Through maturation, cDCs upregulate expression of CD80, CD83, and CD86; increase production of immunostimulatory cytokines (IL-12, TNF- α , IL-10); and increase surface stability and expression of antigenic peptide-MHC complexes [49]. Consequently, cDCs lose their ability to pick up further antigens and eventually become mature immunostimulatory cells and strong activators of naïve CD4⁺ and CD8⁺ T cells via direct antigen presentation [49]. As one can expect, the gene expression patterns dynamically change during the complex process of dendritic cell maturation [50]. CD11c[−] DCs mature using CD40L and IL-3 and do not upregulate genes like *TUBA1A*, *TUBB*, *SPP1*, or *GPNMB* that are typically associated with mature conventional DCs [50]. In accordance, most DC-associated genes such as *MMP12*, *Z39Ig*, *GPNMB*, and *SPP1* are low in immature DCs and increase with maturation. Only a few genes, like *CCL17* in monocyte-derived DCs (detailed below), *HLA-DRA* in all DC subclasses, or *CD1B* in monocytes and CD1a⁺ DCs, have been reported to be constitutively overexpressed in immature DC species [50].

Following exposure to activators like microbes, cDCs secrete pro-inflammatory cytokines like IL-12, IL-23, and IL-10 that, along with surface molecules like OX40-L or ICOS-L, trigger maturation of naïve T cells into their effector Th1, Th2, Treg, or Th17 counterparts [51–55]. IL-12 plays a pivotal role in cDC physiology as it allows them to mature into antigen-presenting cells and elicit their functions [56]. Expression of some of these cytokines, however, shows cell-type specificity like the IL-10 that has been reported to be expressed only in interstitial DCs [57].

cDC1s specialize in cross-presentation and exogenous antigen presentation on MHC class I molecules to activate naïve CD8⁺ T cells that can develop into cytotoxic T lymphocytes. For this activity, cDC1s uniquely express endocytic receptor CLEC9A and chemokine receptor XCR1, which enables antigen capturing, cross-presentation, and T cell activation, respectively [22,58]. cDC2s, in contrast, primarily present antigens on MHC class II molecules to prime naïve CD4⁺ T cells and provide the necessary costimulatory signals [19]. Data indicate that IRF4 regulates the antigen processing capacity and the MHC class II-linked antigen presentation of cDC2s, leading to more robust CD4⁺ T cell proliferation

compared to cDC1s [59]. cDC2 also promotes Th2 and Th17 response in contrast to cDC1s that, under standard physiological conditions, do not promote Th2 responses [60].

Plasmacytoid dendritic cells (pDC) do not express CD11c in humans but are positive for CD123 and CD303 [61–63]. The key transcription factor responsible for pDC development is the E-protein transcription factor E2-2 [64]. pDCs express a range of Toll-like receptors (TLRs), including TLR7/8 and TLR9, which enable them to detect viral nucleic acids, including single-stranded RNAs and unmethylated CpG-rich DNAs [64]. One of the pDC key functions is the rapid secretion of type I interferons (IFN) and promotion of survival of antigen-activated T cells [64,65]. It is believed that the rapid kinetics of pDC activation is mediated by their high secretory capacity and elevated basal expression of transcription factor IRF7 [66]. In contrast to cDCs, pDCs have minimal antigen-presenting abilities [56,67].

The significantly different gene expression profiles of conventional and plasmacytoid DCs underpin the functional differences [50]. Genes highly expressed in myeloid cDCs like *SPP1* (for osteopontin protein), *FTL* (for ferritin L-chain), *TUBA1A* and *TUBB* (for α - and β -tubulin), *ENO1* (for enolase-1), *ANXA2* (for annexin A2), *CCL2*, *CCL13* (for MCP-1 and MCP-4), and *LAMP3* (for DC-LAMP protein) are associated with antigen uptake and processing, lysosomal function, chemotaxis, and cytoskeletal remodeling, reflecting the phagocytic and migratory capacity of these species [50]. Genes preferentially expressed in pDCs, like *IRF4*, in contrast, are rather essential for Type 1 interferon production.

Thus, our current understanding is that DCs play a pivotal role in triggering various immune cascades, while they can also contribute to the maintenance of the inflammatory state via promotion of cytokine-mediated pro-inflammatory signals. These characteristics make them particularly attractive for cellular immunomodulatory therapies.

3. DC Isolation and Culturing

Since DCs represent a small proportion of human blood mononuclear cells; their therapeutic use is believed to require enrichment [68]. Historically, first, this was achieved from peripheral blood mononuclear cells (PBMC) by their separation from lymphocytes, monocytes, and macrophages followed by buoyant density gradient centrifugation using metrizamide as density medium (Figure 4) [68]. DC populations can also be generated from monocyte populations of peripheral blood that can be obtained via various methods. On one hand, monocytes can be purified from PBMC using immunorsetting techniques, which deplete unwanted lymphocyte populations via erythrocyte crosslinking. On the other, they can be purified through cell surface marker-based purification approaches that typically use the combination of antibody-mediated immunomagnetic selections and sterile, closed-system flow cytometric sorting. Alternatively, the size, density, and surface-adherent characteristics of monocytes can also be exploited via counter-flow centrifugal elutriation and their exposure to tissue culture plastics under standard conditions, respectively (Figure 4) [68,69]. Surveying available clinical trials reveals that monocyte enrichment is most commonly performed either by adherence or by counter-flow elutriation, which together constitute the two dominant approaches in current clinical practice. It is noteworthy, however, that data also indicate that preparation techniques influence the immunogenic potency of in vitro generated DCs. Indeed, autologous DC preparations derived from plastic-adherent monocyte populations induced superior T cell proliferation than those DCs that were differentiated from monocytes following CD14⁺ selection [70,71]. Incubating them in the presence of GM-CSF and IL-4 in vitro, isolated monocytes differentiate into immature DCs within 5 to 7 days. Since the final number of DCs depends entirely on the number of monocytes that are far more numerous in the peripheral blood than DCs, this method produces much higher yields of DCs in comparison to isolating naturally

occurring DCs [68]. Independently of the chosen technique, CD83 is routinely used to assess enrichment of mature DC populations [72].

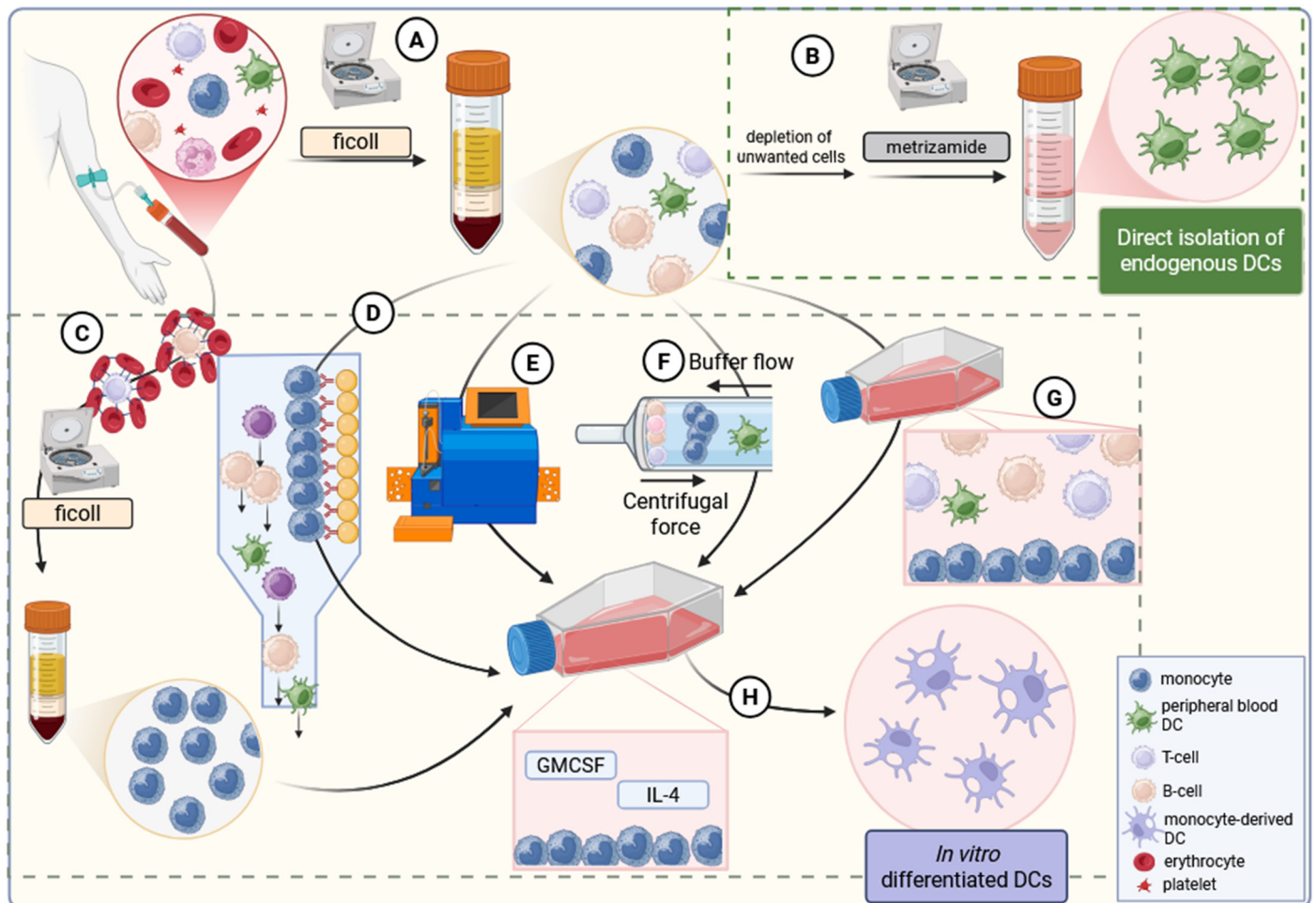


Figure 4. Strategies for dendritic cell enrichment from peripheral blood. (A) Peripheral blood mononuclear cells (PBMC) can be isolated from whole blood via ficoll density gradient centrifugation. (B) From PBMC, circulating DCs can be enriched following the removal of mono- and lymphocytes and metrizamide-based density centrifugation. Alternatively, DCs can be generated in vitro from monocytes. Monocytes can be purified from PBMC via (C) erythrocyte rosetting when lymphocytes are crosslinked to erythrocytes for subsequent removal, (D) by immunomagnetic separation using either negative or positive selection strategies, or (E) with fluorescent activated cell sorting. Monocyte enrichment can also be achieved through (F) centrifugal elutriation or (G) adherence-based selection of monocytes after the removal of non-adherent PBMCs. (H) Isolated monocytes, then, can be differentiated into dendritic cells resulting in a high yield of DCs. The figure was created with Biorender.com.

Following differentiation, exposure to proinflammatory cytokines, like TNF-alpha and IL-1beta or TLR agonists (e.g., LPS, Poly-I:C, R848), for an additional 1–2 days allows differentiated species to obtain their full antigen-presenting functionality, a process termed maturation [68]. In vitro, DCs can be modified before or during their maturation process to enhance their functional properties. Indeed, exposing murine bone marrow-derived DCs to CCL3 and CCL19 leads to an increased and preserved antigen uptake and processing capacity, even after maturation, which then allows a more robust and durable immune response [73]. Moreover, because DCs can phagocytose apoptotic tumor cells and thus allow tumor antigen cross-presentation, they are believed to be able to exert anti-tumor responses following their preconditioning to tumor antigens [74]. Technically, this can be achieved by

peptide-pulsing, co-incubation with tumor cells, or transfection with tumor antigen-related mRNAs [75]. The latter method involves *in vitro*-transcribed mRNAs encoding tumor-associated antigens that, following their intracellular translation and processing, DCs can present on their surface [76]. This MHC-mediated display of immunogenic tumor-specific peptides is believed to enable DCs to effectively activate tumor-specific T cells, initiating a targeted immune response against neoplasms. Another potential benefit of preconditioning is the ability to enhance DC migration from peripheral tissues to lymphoid tissues. It has been shown that PGE2-preconditioned human monocyte-derived DCs have significantly higher CCR7 expression accompanied by an enhanced chemotaxis towards lymph node chemokines CCL19/CCL21 [74,77]. This has been exploited in a number of clinical trials using *ex vivo*-matured DC preparations [78–82].

It is noteworthy, however, that cytokine dosages and quality-control criteria are significantly inconsistent across publications. Similarly, the reported levels of differentiation exhibit up to a two-fold variation, and maturing stimuli also substantially differ between studies. In addition, some studies describe marker expression qualitatively (e.g., ‘low,’ ‘moderate,’ or ‘high’), while others provide a wide range of phenotypic or functional attributes. Sterility requirements are similarly inconsistent; trials usually report results of mycoplasma, endotoxin, Gram staining, or general bacterial contamination without providing specifics of the assays used.

After isolating and culturing, DCs are reported to be suitable for being stored frozen without losing their functionality. Although several cryoprotectants were tested, 10% dimethylsulfoxide (DMSO)-containing freezing media remains the most commonly used one, sometimes reduced to 5% to minimize DMSO-induced cytotoxicity [83–86]. The cryopreservation vehicle generally relies on autologous serum-based formulations, sometimes combined with culture media or human serum albumin to support cellular stability during freezing [87–90]. To further improve post-thaw viability, additives, like glucose in 2–5% final concentration or 12% working concentration of hydroxymethyl starch, are also used alongside DMSO even in GMP-compatible settings [78,91–93]. There are considerable efforts to eliminate DMSO as a cryopreservative; studies have evaluated trehalose and a combination of sucrose, isoleucin, and glycerol, but these approaches remain largely preclinical [94,95]. Despite the relative variety in terms of the cryopreservation medium components, protocols are consistent with the 1 °C per minute freezing until reaching −80 °C. Although the literature data indicate that cryopreserved DCs retain both viability and functionality for at least 24 months even at −80 °C in a solution containing 6% hydroxyethyl starch, 5% dimethyl sulfoxide, and 4% human serum albumin, the industrial standard long-term storage is in liquid nitrogen [96].

Being able to culture them *in vitro* and successively store them for long terms supported the exploration of the use of DCs as tools of the cell-based immunotherapies [73].

4. Therapeutic Use of DCs

Exploration of antigen-presenting cell (APC)-based therapies has led to the registration of the first FDA-approved cellular advanced therapy medicinal product (ATMP) that has the goal to boost the anti-tumor immunity via autologous APCs. Sipuleucel-T is an autologous active cellular immunotherapy approved for the treatment of metastatic castration-resistant prostate cancer [97]. The vaccine consists of the patient’s own peripheral blood mononuclear cells, including APCs, which are *ex vivo* activated using the recombinant PA2024, a fusion protein of prostatic acid phosphatase (a prostate tumor-associated antigen) and GM-CSF [97]. Since the approval of Sipuleucel-T, a number of clinical trials have been exploring the use of antigen-presenting cell-based solutions either as monotherapy or in combination with more canonical chemo-, radio-, or immune checkpoint inhibitor therapies.

A comprehensive list of clinical trials that have already published results is provided in Table S1. More than two hundred clinical trials on the use of APCs have been published or registered to date, and more than 60% have published evaluable data. Despite the diversity in targeted neoplasms and clinical scenarios, there are characteristic principles they commonly share.

One of these is that the vast majority of trials used monocyte-derived species generated by incubation using GM-CSF and IL-4. The mode of monocyte enrichment, concentration of the applied cytokines, and term of differentiation, however, are very diverse, and the latter two factors are, apparently, rather empirical. Monocytes are purified from venous blood-derived mononuclear cells most commonly by exploiting their plastic adherent nature. The second most common technique for monocyte isolation is their immunomagnetic separation exploiting their CD14 positivity, while in a small number of trials monocytes are separated from PBMC by elutriation (Table S1).

In terms of their maturation, protocols are similarly diverse, though they can be classified into few major groups. In a number of trials, DCs are incubated with tumor cells during their maturation, aiming to engage them toward the patient's own tumor cells. This approach has been tested for various cancers with varied outcomes. In a phase I/II trial with stage IV or recurrent melanoma patients, for instance, administration of autologous DCs co-cultured with autologous tumor cells showed excellent long-term outcomes with median overall survival of almost 50 months, with more than 40% of the patients being alive at five years [98]. This concept led to remarkable clinical outcomes in malignant glioma cases, almost doubling the median overall survival time, but failed to deliver similar results in other trials targeting metastatic conditions, probably reflecting on the dynamic nature of cell surface neoantigen repertoire of cancer cells [99–102].

One of the possible solutions to address this challenge is the use of autologous tumor cell lysates for priming the therapeutic DCs population. Interestingly, while this technique seems to be working in melanomas and glioblastomas, it did not improve the clinical outcome of metastatic conditions, for instance, in renal cell carcinomas where this model was studied extensively [103–105].

Similarly, although it significantly decreased PSA levels in prostate cancer patients, autologous DCs preconditioned with apoptotic tumor cell lysates did not improve overall survival despite that it was reported to induce significant CD4⁺ and CD8⁺ T cell proliferation without affecting immunosuppressive FOXP3⁺ regulatory T cells [106]. To improve immunogenicity, autologous tumor cell lysates coupled to immunogenic carriers like yeast wall particles have also been tested and were found to dramatically improve survival of clinically disease-free, stage III/IV melanoma patients upon their vaccination with autologous DCs preconditioned with yeast wall particle-linked lysate, suggesting a possible direction to improve tumor lysate-based protocols [107].

Another regular approach to boost the effectiveness of both the conventional and APC-mediated therapies is the implementation of DC vaccines in traditional chemo- and/or radiotherapy regimes. This has been studied in a number of trials using autologous tumor lysate-pulsed DCs in combination with radio- or chemotherapy, showing successful induction of tumor-specific immunity in glioblastoma patients, resulting in longer survival without major adverse events [108–111].

Another major class of methods to direct DCs against the desired neoplasm is their load with predefined tumor-related proteins or peptides upon their maturation process. These include a wide range of putative tumor antigens from naturally occurring endogenous biomarkers through their fusion formats to synthetic tumor-associated peptides. The immunogenic nature of these peptides has been confirmed in a number of trials. Indeed, successful induction of T cell-mediated anti-tumor immunogenicity has been recorded upon

the use of DCs loaded with peptides from the immune stimulatory T cell receptor alternate reading frame protein (TARP) in prostate cancer patients [112–114]. Similarly, monocyte-derived, conventional, type 1-polarized DCs loaded with synthetic glioma-associated antigen peptides evoked anti-tumor immune responses in nearly two-thirds of malignant glioma patients [115]. This strategy has been widely studied, targeting well-known tumor biomarkers like HER-2, MUC-1, or p53.

HER-2-pulsed DCs have been reported to show clinical benefits in patients bearing HER-2-positive breast cancer, reaching nearly 20% complete elimination of disease or, in the presence of residual cancers, repression of HER-2 expression [116]. Even in metastatic breast neoplasms, administration of HER-2-pulsed DCs showed clinical benefits accompanied with immune activation against HER-2 in around one-third of the patients [117]. An independent randomized double-blind phase II trial involving a larger cohort of glioblastoma patients led to comparable conclusions using autologous DCs pulsed with six synthetic peptide epitopes derived from glioblastoma-associated antigens MAGE-1, IL13R α 2, AIM-2, TRP-2, gp100, and HER-2 [118]. Study results also indicated correlation between the progression-free survival and the tumor HLA pattern, suggesting that HLA profiling of the target tumor tissues might improve the efficiency of DC-based therapeutic approaches.

Interestingly, however, clinical trials applying the preconditioning strategy using HER-2, CEA, WT1, MAGE2, and Survivin antigen-overexpressing apoptotic tumor cells did not show comparable efficiency in lung cancer patients, raising the question of whether implementation of the use of DCs can deliver similar clinical advantages in distinct cancer types [119]. Indeed, when metastatic colorectal cancer patients were exposed to DC isolates expressing MUC-1, an O-glycosylated membrane-bound protein that plays an essential role in forming protective mucous barriers on epithelial surfaces, DC-treated patients had higher survival rates [120]. However, when another MUC-1-preconditioned DC isolate was used in ovarian cancer patients, no significant improvement of their progression-free survival was observed [121]. Similarly, modest or no clear, universal clinical benefits have been recorded upon the use of TP53-overexpressing DC in both a small cell lung cancer and a heterogeneous cancer cohort trial, either as a standalone treatment or along with the indoleamine 2,3-dioxygenase (IDO) inhibitor indoximod, respectively [122,123].

A variation of the peptide-mediated maturation of DCs is the forced endogenous expression of the desired tumor-associated protein following electroporation, transfection, or transduction. An example of these studies examined the use of antigen-loaded autologous dendritic cells in combination with traditional cytostatic monotherapy in castration-resistant metastatic prostate cancer [124,125]. In this trial, autologous monocytes were matured into DCs by transfections with mRNAs encoding PSA, the prostate tumor-associated antigen Prostatic Acid Phosphatase (PAP), Survivin, and hTERT. Patients were treated either with chemotherapy alone or in combination with DCs, and data indicate that 23% more patients showed decline in serum prostate-specific antigen (PSA) levels, a liquid biopsy measure of the tumor progression, in response to the combinatorial autologous DC treatment compared to chemotherapy alone [124,125].

Besides classical radio- and/or chemotherapy, more recent platforms have also been tested in combination with DCs. For instance, autologous DCs targeting vascular antigens in combination with the tyrosine kinase inhibitor dasatinib were tested in patients suffering from immune checkpoint inhibitor-refractory melanoma, showing nearly half of the patients showed immunological and clinical responses [126]. In contrast, however, clinical evaluation of the putative synergy between the anti-PD-L1 monoclonal antibody-based immunotherapy and the use of autologous DCs in metastatic colorectal cancer patients resulted in only modest clinical benefits, highlighting the importance of further refinements

of clinical criteria and type of DC isolates to be applied upon the use of DCs in oncology treatments [80].

Finally, some study results suggest that the route of administration of DC isolates may also impact the clinical response, apparently, in a cancer-type specific manner. Indeed, intratumoral DC injections of soft tissue sarcomas have been reported to lead to long-term disease control [127]. The same application of pre-activated allogeneic DCs in patients suffering from metastatic renal cell carcinoma, however, led to ambiguous results, with some patients having increased CD8⁺ T cell infiltration in the tumors and others showing no objective tumor response at all [104].

5. Discussion

Advances in anti-cancer immunotherapy have fundamentally been reforming clinical oncology in the past decade. At the frontline of this paradigm shift is the implementation of immune checkpoint inhibitors (ICI) into the clinical practice that aim to uplift the tumor cell-mediated molecular blockade on the endogenous anti-tumor activity of the patient's immune system [128]. Despite the great results of their use in certain clinical settings, like some hematological tumors or melanomas, the introduction of ICI therapy did not solve the problem of human neoplasms like gliomas or pancreatic cancer [129–132]. Moreover, even some initially responding conditions develop resistance to ICI over time, underlining the limitations of this approach [133]. In addition, while their use in monotherapy shows clinical benefit in just approximately 20% of the patients, the combinatorial use of ICI is often limited due to the higher risk of severe, sometime fatal, autoimmune complications that can occur even after months of their administration [134,135]. These challenges suggest that to achieve the effective but safe activation of the cytotoxic T lymphocyte-mediated anti-tumor activity in distinct clinical scenarios, complementary approaches might be implemented in the ICI-based therapeutic regimes. These could be the APC-based approaches that are predominantly relied on for the use of various dendritic cell preparations.

Indeed, the central role of dendritic cells in the activation of immune effector species prompted the concept of their use in clinical applications. The relative scarcity of them in the circulation, however, hindered the swift implementation of endogenous DCs in clinical immunotherapy, calling for the development of *in vitro* solutions like the monocyte-derived autologous DC preparations. These have been extensively studied in both adult and pediatric clinical settings in recent years with promising, although sometimes ambiguous, results, so their genuine efficacy is still to be determined [136–140]. One of the most important steps in this task seems to be the standardization of protocols applied since current clinical data are incompatible to one another due to the diversity of the application routes, patient cohorts, and, probably most importantly, the DC preparations used in past clinical trials.

Indeed, the more accurate identification of DC subtypes suitable for anti-cancer applications in distinct clinical settings is a critical question to be solved. Increased amounts of plasmacytoid DCs, for instance, seem to correlate with better prognoses among pancreatic cancer patients, while they are rather associated with worse prognosis in breast cancer, hepatocellular cancer, melanoma, and ovarian cancer [141–145]. However, observations that worse prognoses show association with the expression of inhibitory markers like the lymphocyte-activation gene 3 (LAG-3), PD-1, and CTLA-4, immunosuppressive cytokines like IL-10 and TGF- β , and the accumulation of regulatory T cells raise the question of whether the use of ICI in these cases supports APC-mediated actions and enhances the therapeutic effect of *ex vivo*-raised APCs [141,146–148]. This is a particularly interesting question considering the observations that the long-term DC-mediated anti-tumor immu-

nity, at least in certain clinical settings, is, apparently, rather mediated by NK- than T cell populations upon some combinatorial treatments [149].

Moreover, while the majority of contemporary studies use in vitro-raised, monocyte-derived DCs, some data suggest that neogenesis of DCs for therapeutic purposes is not always the clinically most efficient solution. A randomized trial that aimed to evaluate clinical and immune responses to a multi-peptide-preconditioned DC preparation in melanoma patients showed that the use of in vitro-generated DCs along with the administration of GM-CSF produced stronger T cell responses and more clinical tumor regressions compared to the standalone administration of dendritic cells [150]. The potential benefits of the mobilization of endogenous DC populations have further been strengthened by the report showing enhanced T cell and antibody responses upon the use of FMS-like tyrosine kinase 3 ligand (FLT3L), a known cytokine stimulating DC progenitors, in patients with resected melanoma [151–153]. These data indicate that more details are needed on the environmental factors that support the genesis of DCs that can, then, effectively support anti-tumor immunity.

Independently of their origin, the ultimate goal of the use DCs is the activation of the anti-neoplastic immunity via antigen presentation to immunocompetent elements. One of the major disadvantages of the mobilization of endogenous DCs is the lack of control over their tumor antigen recognition, internalization, and presentation. To address this challenge, various efforts have been made to expose ex vivo-raised DCs to a wide range of possible antigens, from purified known tumor antigens to complex tumor cell lysates [102,154]. The disadvantage of the former method is that it cannot adapt to the dynamic antigen landscape of tumors, while the latter solution requires tumor material. These issues call for further developments like the one recently published by Ghasemi et al., who successfully enhanced anti-tumor immunity in melanoma mouse models using DC progenitors engineered to internalize cancer cell-released extracellular vesicles for facilitating more effective in vivo tumor antigen presentation without the need to know the exact tumor antigens or have cancerous tissue to be lysed available [155].

6. Conclusions

Despite the broadly accepted practical potential of the concept of anti-cancer immunotherapy, its widespread clinical breakthrough is yet to fully unfold. It seems to be, now, clear that the use of measures like immune checkpoint inhibitors or genetically engineered T lymphocytes in monotherapy have limitations that shifted the focus of current innovations toward the combinatorial use of immunotherapy tools. This fueled a number of trials on dendritic cells resulting in variable, sometime even contradicting reports on the clinical outcome. Reviewing published data, apparently this is due to a number of factors, including the diversity of clinical trial concepts, difficult and often very limited patient cohorts, or the incomparable techniques of interventions applied [79,122,156]. Considering the heterogeneous nature of both the endogenous and ex vivo-generated dendritic cell populations, the latter issue seems to be the key problem for the appropriate assessment of the clinical benefit of DCs in immunotherapy. This challenge would certainly profit from an optimized and, at least to a certain extent, standardized consensual protocol of ex vivo manipulations including isolation, differentiation, and maturation. In addition, current discrepancies in quality-control assessments and sterility testing in monocyte-derived dendritic cell-based therapies underscore the critical need for harmonized manufacturing protocols and standardized phenotypic and functional characterization panels that would enhance reproducibility and enable more meaningful cross-trial comparisons.

Supplementary Materials: The following supporting information can be downloaded at <https://www.mdpi.com/article/10.3390/cancers18010123/s1>. Table S1: Summary of clinical trials investigating the use of dendritic cells in clinical settings reported with accessible study results to date [157–237].

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References

1. Bray, F.; Laversanne, M.; Sung, H.; Ferlay, J.; Siegel, R.L.; Soerjomataram, I.; Jemal, A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J. Clin.* **2024**, *74*, 229–263. [\[CrossRef\]](#)
2. Bray, F.; Laversanne, M.; Weiderpass, E.; Soerjomataram, I. The ever-increasing importance of cancer as a leading cause of premature death worldwide. *Cancer* **2021**, *127*, 3029–3030. [\[CrossRef\]](#) [\[PubMed\]](#)
3. Aktipis, C.A.; Nesse, R.M. Evolutionary foundations for cancer biology. *Evol. Appl.* **2013**, *6*, 144–159. [\[CrossRef\]](#) [\[PubMed\]](#)
4. Bajtai, E.; Kiss, C.; Bakos, E.; Lango, T.; Lovrics, A.; Schad, E.; Tisza, V.; Hegedus, K.; Furjes, P.; Szabo, Z.; et al. Therapy-induced senescence is a transient drug resistance mechanism in breast cancer. *Mol. Cancer* **2025**, *24*, 128. [\[CrossRef\]](#) [\[PubMed\]](#)
5. Sharma, A.; Jasrotia, S.; Kumar, A. Effects of Chemotherapy on the Immune System: Implications for Cancer Treatment and Patient Outcomes. *Naunyn-Schmiedeberg's Arch. Pharmacol.* **2024**, *397*, 2551–2566. [\[CrossRef\]](#)
6. Mun, J.; Lim, B. The hallmarks of tissue-agnostic therapies and strategies for early anticancer drug discovery. *Drug Discov. Today* **2024**, *29*, 104203. [\[CrossRef\]](#)
7. Danesi, R.; Fogli, S.; Indraccolo, S.; Del Re, M.; Dei Tos, A.P.; Leoncini, L.; Antonuzzo, L.; Bonanno, L.; Guarneri, V.; Pierini, A.; et al. Druggable targets meet oncogenic drivers: Opportunities and limitations of target-based classification of tumors and the role of Molecular Tumor Boards. *ESMO Open* **2021**, *6*, 100040. [\[CrossRef\]](#)
8. Flaherty, K.T.; Le, D.T.; Lemery, S. Tissue-Agnostic Drug Development. *Am. Soc. Clin. Oncol. Educ. Book.* **2017**, *37*, 222–230. [\[CrossRef\]](#)
9. Wu, S.; Thawani, R. Tumor-Agnostic Therapies in Practice: Challenges, Innovations, and Future Perspectives. *Cancers* **2025**, *17*, 801. [\[CrossRef\]](#)
10. Tan, S.; Li, D.; Zhu, X. Cancer immunotherapy: Pros, cons and beyond. *Biomed. Pharmacother.* **2020**, *124*, 109821. [\[CrossRef\]](#)
11. Kaufman, H.L.; Atkins, M.B.; Subedi, P.; Wu, J.; Chambers, J.; Joseph Mattingly, T., 2nd; Campbell, J.D.; Allen, J.; Ferris, A.E.; Schilsky, R.L.; et al. The promise of Immuno-oncology: Implications for defining the value of cancer treatment. *J. Immunother. Cancer* **2019**, *7*, 129. [\[CrossRef\]](#) [\[PubMed\]](#)
12. Hammerl, D.; Martens, J.W.M.; Timmermans, M.; Smid, M.; Trapman-Jansen, A.M.; Foekens, R.; Isaeva, O.I.; Voorwerk, L.; Balcioglu, H.E.; Wijers, R.; et al. Spatial immunophenotypes predict response to anti-PD1 treatment and capture distinct paths of T cell evasion in triple negative breast cancer. *Nat. Commun.* **2021**, *12*, 5668. [\[CrossRef\]](#) [\[PubMed\]](#)
13. Steinman, R.M.; Cohn, Z.A. Identification of a novel cell type in peripheral lymphoid organs of mice. I. Morphology, quantitation, tissue distribution. *J. Exp. Med.* **1973**, *137*, 1142–1162. [\[CrossRef\]](#) [\[PubMed\]](#)
14. Breton, G.; Lee, J.; Liu, K.; Nussenzweig, M.C. Defining human dendritic cell progenitors by multiparametric flow cytometry. *Nat. Protoc.* **2015**, *10*, 1407–1422. [\[CrossRef\]](#)
15. Nussenzweig, M.C.; Steinman, R.M.; Unkeless, J.C.; Witmer, M.D.; Gutchinov, B.; Cohn, Z.A. Studies of the cell surface of mouse dendritic cells and other leukocytes. *J. Exp. Med.* **1981**, *154*, 168–187. [\[CrossRef\]](#)
16. Nussenzweig, M.C.; Steinman, R.M.; Witmer, M.D.; Gutchinov, B. A monoclonal antibody specific for mouse dendritic cells. *Proc. Natl. Acad. Sci. USA* **1982**, *79*, 161–165. [\[CrossRef\]](#)
17. Sichien, D.; Scott, C.L.; Martens, L.; Vanderkerken, M.; Van Gassen, S.; Plantinga, M.; Joeris, T.; De Prijs, S.; Vanhoutte, L.; Vanheerswynghe, M.; et al. IRF8 Transcription Factor Controls Survival and Function of Terminally Differentiated Conventional and Plasmacytoid Dendritic Cells, Respectively. *Immunity* **2016**, *45*, 626–640. [\[CrossRef\]](#)

18. Jongbloed, S.L.; Kassianos, A.J.; McDonald, K.J.; Clark, G.J.; Ju, X.; Angel, C.E.; Chen, C.J.; Dunbar, P.R.; Wadley, R.B.; Jeet, V.; et al. Human CD141+ (BDCA-3)+ dendritic cells (DCs) represent a unique myeloid DC subset that cross-presents necrotic cell antigens. *J. Exp. Med.* **2010**, *207*, 1247–1260. [[CrossRef](#)]
19. Anderson, D.A., 3rd; Murphy, K.M.; Brisen, C.G. Development, Diversity, and Function of Dendritic Cells in Mouse and Human. *Cold Spring Harb. Perspect. Biol.* **2018**, *10*, a028613. [[CrossRef](#)]
20. Schlitzer, A.; McGovern, N.; Teo, P.; Zelante, T.; Atarashi, K.; Low, D.; Ho, A.W.; See, P.; Shin, A.; Wasan, P.S.; et al. IRF4 transcription factor-dependent CD11b+ dendritic cells in human and mouse control mucosal IL-17 cytokine responses. *Immunity* **2013**, *38*, 970–983. [[CrossRef](#)]
21. Bachem, A.; Guttler, S.; Hartung, E.; Ebstein, F.; Schaefer, M.; Tannert, A.; Salama, A.; Movassaghi, K.; Opitz, C.; Mages, H.W.; et al. Superior antigen cross-presentation and XCR1 expression define human CD11c+CD141+ cells as homologues of mouse CD8+ dendritic cells. *J. Exp. Med.* **2010**, *207*, 1273–1281. [[CrossRef](#)] [[PubMed](#)]
22. Hildner, K.; Edelson, B.T.; Purtha, W.E.; Diamond, M.; Matsushita, H.; Kohyama, M.; Calderon, B.; Schraml, B.U.; Unanue, E.R.; Diamond, M.S.; et al. Batf3 deficiency reveals a critical role for CD8alpha+ dendritic cells in cytotoxic T cell immunity. *Science* **2008**, *322*, 1097–1100. [[CrossRef](#)] [[PubMed](#)]
23. Ichikawa, E.; Hida, S.; Omatsu, Y.; Shimoyama, S.; Takahara, K.; Miyagawa, S.; Inaba, K.; Taki, S. Defective development of splenic and epidermal CD4+ dendritic cells in mice deficient for IFN regulatory factor-2. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 3909–3914. [[CrossRef](#)] [[PubMed](#)]
24. Suzuki, S.; Honma, K.; Matsuyama, T.; Suzuki, K.; Toriyama, K.; Akitoyo, I.; Yamamoto, K.; Suematsu, T.; Nakamura, M.; Yui, K.; et al. Critical roles of interferon regulatory factor 4 in CD11bhighCD8alpha- dendritic cell development. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 8981–8986. [[CrossRef](#)]
25. Steinman, R.M.; Cohn, Z.A. Identification of a novel cell type in peripheral lymphoid organs of mice. II. Functional properties in vitro. *J. Exp. Med.* **1974**, *139*, 380–397. [[CrossRef](#)]
26. Sallusto, F.; Cella, M.; Danieli, C.; Lanzavecchia, A. Dendritic cells use macropinocytosis and the mannose receptor to concentrate macromolecules in the major histocompatibility complex class II compartment: Downregulation by cytokines and bacterial products. *J. Exp. Med.* **1995**, *182*, 389–400. [[CrossRef](#)]
27. de Baey, A.; Lanzavecchia, A. The role of aquaporins in dendritic cell macropinocytosis. *J. Exp. Med.* **2000**, *191*, 743–748. [[CrossRef](#)]
28. Anderson, C.L.; Shen, L.; Eicher, D.M.; Wewers, M.D.; Gill, J.K. Phagocytosis mediated by three distinct Fc gamma receptor classes on human leukocytes. *J. Exp. Med.* **1990**, *171*, 1333–1345. [[CrossRef](#)]
29. Griffin, F.M., Jr.; Bianco, C.; Silverstein, S.C. Characterization of the macrophage receptor for complement and demonstration of its functional independence from the receptor for the Fc portion of immunoglobulin G. *J. Exp. Med.* **1975**, *141*, 1269–1277. [[CrossRef](#)]
30. Becker, M.; Cotena, A.; Gordon, S.; Platt, N. Expression of the class A macrophage scavenger receptor on specific subpopulations of murine dendritic cells limits their endotoxin response. *Eur. J. Immunol.* **2006**, *36*, 950–960. [[CrossRef](#)]
31. Desjardins, M.; Huber, L.A.; Parton, R.G.; Griffiths, G. Biogenesis of phagolysosomes proceeds through a sequential series of interactions with the endocytic apparatus. *J. Cell Biol.* **1994**, *124*, 677–688. [[CrossRef](#)] [[PubMed](#)]
32. Lautwein, A.; Burster, T.; Lennon-Dumenil, A.M.; Overkleeft, H.S.; Weber, E.; Kalbacher, H.; Driessen, C. Inflammatory stimuli recruit cathepsin activity to late endosomal compartments in human dendritic cells. *Eur. J. Immunol.* **2002**, *32*, 3348–3357. [[CrossRef](#)] [[PubMed](#)]
33. Denzin, L.K.; Cresswell, P. HLA-DM induces CLIP dissociation from MHC class II alpha beta dimers and facilitates peptide loading. *Cell* **1995**, *82*, 155–165. [[CrossRef](#)] [[PubMed](#)]
34. Pierre, P.; Turley, S.J.; Gatti, E.; Hull, M.; Meltzer, J.; Mirza, A.; Inaba, K.; Steinman, R.M.; Mellman, I. Developmental regulation of MHC class II transport in mouse dendritic cells. *Nature* **1997**, *388*, 787–792. [[CrossRef](#)]
35. Rock, K.L.; Gramm, C.; Rothstein, L.; Clark, K.; Stein, R.; Dick, L.; Hwang, D.; Goldberg, A.L. Inhibitors of the proteasome block the degradation of most cell proteins and the generation of peptides presented on MHC class I molecules. *Cell* **1994**, *78*, 761–771. [[CrossRef](#)]
36. Van Kaer, L.; Ashton-Rickardt, P.G.; Ploegh, H.L.; Tonegawa, S. TAP1 mutant mice are deficient in antigen presentation, surface class I molecules, and CD4+ T cells. *Cell* **1992**, *71*, 1205–1214. [[CrossRef](#)]
37. Ortmann, B.; Copeman, J.; Lehner, P.J.; Sadasivan, B.; Herberg, J.A.; Grandea, A.G.; Riddell, S.R.; Tampe, R.; Spies, T.; Trowsdale, J.; et al. A critical role for tapasin in the assembly and function of multimeric MHC class I-TAP complexes. *Science* **1997**, *277*, 1306–1309. [[CrossRef](#)]
38. Lippincott-Schwartz, J.; Yuan, L.C.; Bonifacino, J.S.; Klausner, R.D. Rapid redistribution of Golgi proteins into the ER in cells treated with brefeldin A: Evidence for membrane cycling from Golgi to ER. *Cell* **1989**, *56*, 801–813. [[CrossRef](#)]
39. Garboczi, D.N.; Ghosh, P.; Utz, U.; Fan, Q.R.; Biddison, W.E.; Wiley, D.C. Structure of the complex between human T-cell receptor, viral peptide and HLA-A2. *Nature* **1996**, *384*, 134–141. [[CrossRef](#)]

40. Grakoui, A.; Bromley, S.K.; Sumen, C.; Davis, M.M.; Shaw, A.S.; Allen, P.M.; Dustin, M.L. The immunological synapse: A molecular machine controlling T cell activation. *Science* **1999**, *285*, 221–227. [[CrossRef](#)]
41. Inaba, K.; Witmer-Pack, M.; Inaba, M.; Hathcock, K.S.; Sakuta, H.; Azuma, M.; Yagita, H.; Okumura, K.; Linsley, P.S.; Ikehara, S.; et al. The tissue distribution of the B7-2 costimulator in mice: Abundant expression on dendritic cells in situ and during maturation in vitro. *J. Exp. Med.* **1994**, *180*, 1849–1860. [[CrossRef](#)]
42. Bevan, M.J. Cross-priming for a secondary cytotoxic response to minor H antigens with H-2 congenic cells which do not cross-react in the cytotoxic assay. *J. Exp. Med.* **1976**, *143*, 1283–1288. [[CrossRef](#)] [[PubMed](#)]
43. Shen, L.; Sigal, L.J.; Boes, M.; Rock, K.L. Important role of cathepsin S in generating peptides for TAP-independent MHC class I crosspresentation in vivo. *Immunity* **2004**, *21*, 155–165. [[CrossRef](#)] [[PubMed](#)]
44. Kovacsovics-Bankowski, M.; Rock, K.L. A phagosome-to-cytosol pathway for exogenous antigens presented on MHC class I molecules. *Science* **1995**, *267*, 243–246. [[CrossRef](#)] [[PubMed](#)]
45. Palmowski, M.J.; Gileadi, U.; Salio, M.; Gallimore, A.; Millrain, M.; James, E.; Addey, C.; Scott, D.; Dyson, J.; Simpson, E.; et al. Role of immunoproteasomes in cross-presentation. *J. Immunol.* **2006**, *177*, 983–990. [[CrossRef](#)]
46. Ackerman, A.L.; Kyritsis, C.; Tampe, R.; Cresswell, P. Early phagosomes in dendritic cells form a cellular compartment sufficient for cross presentation of exogenous antigens. *Proc. Natl. Acad. Sci. USA* **2003**, *100*, 12889–12894. [[CrossRef](#)]
47. Guermónprez, P.; Saveanu, L.; Kleijmeer, M.; Davoust, J.; Van Endert, P.; Amigorena, S. ER-phagosome fusion defines an MHC class I cross-presentation compartment in dendritic cells. *Nature* **2003**, *425*, 397–402. [[CrossRef](#)]
48. Schafer, S.; Chen, K.; Ma, L. Crosstalk with Dendritic Cells: A Path to Engineer Advanced T Cell Immunotherapy. *Front. Syst. Biol.* **2024**, *4*, 1372995. [[CrossRef](#)]
49. Sallusto, F.; Lanzavecchia, A. Efficient presentation of soluble antigen by cultured human dendritic cells is maintained by granulocyte/macrophage colony-stimulating factor plus interleukin 4 and downregulated by tumor necrosis factor alpha. *J. Exp. Med.* **1994**, *179*, 1109–1118. [[CrossRef](#)]
50. Ahn, J.H.; Lee, Y.; Jeon, C.; Lee, S.J.; Lee, B.H.; Choi, K.D.; Bae, Y.S. Identification of the genes differentially expressed in human dendritic cell subsets by cDNA subtraction and microarray analysis. *Blood* **2002**, *100*, 1742–1754. [[CrossRef](#)]
51. Why and how to find neutral ligands targeting chemokines? *Drug Discov. Today Technol.* **2012**, *9*, e227–314. [[CrossRef](#)]
52. Pizarro, T.T.; Cominelli, F. Cloning IL-1 and the birth of a new era in cytokine biology. *J. Immunol.* **2007**, *178*, 5411–5412. [[CrossRef](#)] [[PubMed](#)]
53. Janeway, C.A., Jr.; Yagi, J.; Conrad, P.J.; Katz, M.E.; Jones, B.; Vroegop, S.; Buxser, S. T-cell responses to MIs and to bacterial proteins that mimic its behavior. *Immunol. Rev.* **1989**, *107*, 61–88. [[CrossRef](#)] [[PubMed](#)]
54. Flynn, S.; Toellner, K.M.; Raykundalia, C.; Goodall, M.; Lane, P. CD4 T cell cytokine differentiation: The B cell activation molecule, OX40 ligand, instructs CD4 T cells to express interleukin 4 and upregulates expression of the chemokine receptor, Blnr-1. *J. Exp. Med.* **1998**, *188*, 297–304. [[CrossRef](#)]
55. Ito, T.; Yang, M.; Wang, Y.H.; Lande, R.; Gregorio, J.; Perng, O.A.; Qin, X.F.; Liu, Y.J.; Gilliet, M. Plasmacytoid dendritic cells prime IL-10-producing T regulatory cells by inducible costimulator ligand. *J. Exp. Med.* **2007**, *204*, 105–115. [[CrossRef](#)]
56. Piqueras, B.; Connolly, J.; Freitas, H.; Palucka, A.K.; Banchereau, J. Upon viral exposure, myeloid and plasmacytoid dendritic cells produce 3 waves of distinct chemokines to recruit immune effectors. *Blood* **2006**, *107*, 2613–2618. [[CrossRef](#)]
57. de Saint-Vis, B.; Fugier-Vivier, I.; Massacrier, C.; Gaillard, C.; Vanbervliet, B.; Ait-Yahia, S.; Banchereau, J.; Liu, Y.J.; Lebecque, S.; Caux, C. The cytokine profile expressed by human dendritic cells is dependent on cell subtype and mode of activation. *J. Immunol.* **1998**, *160*, 1666–1676. [[CrossRef](#)]
58. Dorner, B.G.; Dorner, M.B.; Zhou, X.; Opitz, C.; Mora, A.; Guttler, S.; Hutloff, A.; Mages, H.W.; Ranke, K.; Schaefer, M.; et al. Selective expression of the chemokine receptor XCR1 on cross-presenting dendritic cells determines cooperation with CD8+ T cells. *Immunity* **2009**, *31*, 823–833. [[CrossRef](#)]
59. Binnewies, M.; Mujal, A.M.; Pollack, J.L.; Combes, A.J.; Hardison, E.A.; Barry, K.C.; Tsui, J.; Ruhland, M.K.; Kersten, K.; Abushawish, M.A.; et al. Unleashing Type-2 Dendritic Cells to Drive Protective Antitumor CD4(+) T Cell Immunity. *Cell* **2019**, *177*, 556–571.e16. [[CrossRef](#)]
60. Izumi, G.; Nakano, H.; Nakano, K.; Whitehead, G.S.; Grimm, S.A.; Fessler, M.B.; Karmaus, P.W.; Cook, D.N. CD11b(+) lung dendritic cells at different stages of maturation induce Th17 or Th2 differentiation. *Nat. Commun.* **2021**, *12*, 5029. [[CrossRef](#)]
61. MacDonald, K.P.; Munster, D.J.; Clark, G.J.; Dzionek, A.; Schmitz, J.; Hart, D.N. Characterization of human blood dendritic cell subsets. *Blood* **2002**, *100*, 4512–4520. [[CrossRef](#)] [[PubMed](#)]
62. Rock, J.; Schneider, E.; Grun, J.R.; Grutzkau, A.; Kuppers, R.; Schmitz, J.; Winkels, G. CD303 (BDCA-2) signals in plasmacytoid dendritic cells via a BCR-like signalosome involving Syk, SLP65 and PLCgamma2. *Eur. J. Immunol.* **2007**, *37*, 3564–3575. [[CrossRef](#)] [[PubMed](#)]
63. Ju, X.; Zenke, M.; Hart, D.N.; Clark, G.J. CD300a/c regulate type I interferon and TNF-alpha secretion by human plasmacytoid dendritic cells stimulated with TLR7 and TLR9 ligands. *Blood* **2008**, *112*, 1184–1194. [[CrossRef](#)] [[PubMed](#)]

64. Cisse, B.; Caton, M.L.; Lehner, M.; Maeda, T.; Scheu, S.; Locksley, R.; Holmberg, D.; Zweier, C.; den Hollander, N.S.; Kant, S.G.; et al. Transcription factor E2-2 is an essential and specific regulator of plasmacytoid dendritic cell development. *Cell* **2008**, *135*, 37–48. [\[CrossRef\]](#)
65. Cella, M.; Jarrossay, D.; Facchetti, F.; Alebardi, O.; Nakajima, H.; Lanzavecchia, A.; Colonna, M. Plasmacytoid monocytes migrate to inflamed lymph nodes and produce large amounts of type I interferon. *Nat. Med.* **1999**, *5*, 919–923. [\[CrossRef\]](#)
66. Barchet, W.; Cella, M.; Odermatt, B.; Asselin-Paturel, C.; Colonna, M.; Kalinke, U. Virus-induced interferon alpha production by a dendritic cell subset in the absence of feedback signaling in vivo. *J. Exp. Med.* **2002**, *195*, 507–516. [\[CrossRef\]](#)
67. Siegal, F.P.; Kadowaki, N.; Shodell, M.; Fitzgerald-Bocarsly, P.A.; Shah, K.; Ho, S.; Antonenko, S.; Liu, Y.J. The nature of the principal type 1 interferon-producing cells in human blood. *Science* **1999**, *284*, 1835–1837. [\[CrossRef\]](#)
68. Nair, S.; Archer, G.E.; Tedder, T.F. Isolation and generation of human dendritic cells. *Curr. Protoc. Immunol.* **2012**, *99*, 7–23. [\[CrossRef\]](#)
69. Berger, T.G.; Strasser, E.; Smith, R.; Carste, C.; Schuler-Thurner, B.; Kaempgen, E.; Schuler, G. Efficient elutriation of monocytes within a closed system (Elutra) for clinical-scale generation of dendritic cells. *J. Immunol. Methods* **2005**, *298*, 61–72. [\[CrossRef\]](#)
70. Zhou, L.; Somasundaram, R.; Nederhof, R.F.; Dijkstra, G.; Faber, K.N.; Peppelenbosch, M.P.; Fuhler, G.M. Impact of human granulocyte and monocyte isolation procedures on functional studies. *Clin. Vaccine Immunol.* **2012**, *19*, 1065–1074. [\[CrossRef\]](#)
71. Frank, M.O.; Kaufman, J.; Parveen, S.; Blachere, N.E.; Orange, D.E.; Darnell, R.B. Dendritic cell vaccines containing lymphocytes produce improved immunogenicity in patients with cancer. *J. Transl. Med.* **2014**, *12*, 338. [\[CrossRef\]](#)
72. Zhou, L.J.; Tedder, T.F. Human blood dendritic cells selectively express CD83, a member of the immunoglobulin superfamily. *J. Immunol.* **1995**, *154*, 3821–3835. [\[CrossRef\]](#) [\[PubMed\]](#)
73. Sexton, A.; Whitney, P.G.; Chong, S.F.; Zelikin, A.N.; Johnston, A.P.; De Rose, R.; Brooks, A.G.; Caruso, F.; Kent, S.J. A protective vaccine delivery system for in vivo T cell stimulation using nanoengineered polymer hydrogel capsules. *ACS Nano* **2009**, *3*, 3391–3400. [\[CrossRef\]](#) [\[PubMed\]](#)
74. Feng, H.; Zeng, Y.; Graner, M.W.; Likhacheva, A.; Katsanis, E. Exogenous stress proteins enhance the immunogenicity of apoptotic tumor cells and stimulate antitumor immunity. *Blood* **2003**, *101*, 245–252. [\[CrossRef\]](#) [\[PubMed\]](#)
75. Yamanaka, R.; Abe, T.; Yajima, N.; Tsuchiya, N.; Homma, J.; Kobayashi, T.; Narita, M.; Takahashi, M.; Tanaka, R. Vaccination of recurrent glioma patients with tumour lysate-pulsed dendritic cells elicits immune responses: Results of a clinical phase I/II trial. *Br. J. Cancer* **2003**, *89*, 1172–1179. [\[CrossRef\]](#)
76. Batich, K.A.; Swartz, A.M.; Sampson, J.H. Preconditioning Vaccine Sites for mRNA-Transfected Dendritic Cell Therapy and Antitumor Efficacy. *Methods Mol. Biol.* **2016**, *1403*, 819–838. [\[CrossRef\]](#)
77. Scandella, E.; Men, Y.; Gillesen, S.; Forster, R.; Groettrup, M. Prostaglandin E2 is a key factor for CCR7 surface expression and migration of monocyte-derived dendritic cells. *Blood* **2002**, *100*, 1354–1361. [\[CrossRef\]](#)
78. Van Driessche, A.; Van de Velde, A.L.; Nijs, G.; Braeckman, T.; Stein, B.; De Vries, J.M.; Berneman, Z.N.; Van Tendeloo, V.F. Clinical-grade manufacturing of autologous mature mRNA-electroporated dendritic cells and safety testing in acute myeloid leukemia patients in a phase I dose-escalation clinical trial. *Cytotherapy* **2009**, *11*, 653–668. [\[CrossRef\]](#)
79. Um, S.J.; Choi, Y.J.; Shin, H.J.; Son, C.H.; Park, Y.S.; Roh, M.S.; Kim, Y.S.; Kim, Y.D.; Lee, S.K.; Jung, M.H.; et al. Phase I study of autologous dendritic cell tumor vaccine in patients with non-small cell lung cancer. *Lung Cancer* **2010**, *70*, 188–194. [\[CrossRef\]](#)
80. Espanol-Rego, M.; Fernandez-Martos, C.; Elez, E.; Foguet, C.; Pedrosa, L.; Rodriguez, N.; Ruiz-Casado, A.; Pineda, E.; Cid, J.; Cabezon, R.; et al. A Phase I-II multicenter trial with Avelumab plus autologous dendritic cell vaccine in pre-treated mismatch repair-proficient (MSS) metastatic colorectal cancer patients; GEMCAD 1602 study. *Cancer Immunol. Immunother.* **2023**, *72*, 827–840. [\[CrossRef\]](#)
81. Ridolfi, L.; Gurrieri, L.; Riva, N.; Bulgarelli, J.; De Rosa, F.; Guidoboni, M.; Fausti, V.; Ranallo, N.; Calpona, S.; Tazzari, M.; et al. First step results from a phase II study of a dendritic cell vaccine in glioblastoma patients (CombiG-vax). *Front. Immunol.* **2024**, *15*, 1404861. Erratum in *Front. Immunol.* **2024**, *19*, 1494021. <https://doi.org/10.3389/fimmu.2024.1494021>. [\[CrossRef\]](#) [\[PubMed\]](#)
82. Kucukcelebi, S.; van 't Land, F.R.; van der Burg, S.H.; Eskens, F.; Homs, M.Y.V.; Willemsen, M.; Onrust-van Schoonhoven, A.; Rozendaal, N.E.M.; Fellah, A.; Vadgama, D.; et al. REACTiVe-2: Phase I evaluation of dendritic cell vaccination and agonistic CD40 therapy following (m)FOLFIRINOX in metastatic pancreatic cancer. *Nat. Commun.* **2025**, *16*, 10609. [\[CrossRef\]](#) [\[PubMed\]](#)
83. Podrazil, M.; Horvath, R.; Becht, E.; Rozkova, D.; Bilkova, P.; Sochorova, K.; Hromadkova, H.; Kayserova, J.; Vavrova, K.; Lastovicka, J.; et al. Phase I/II clinical trial of dendritic-cell based immunotherapy (DCVAC/PCa) combined with chemotherapy in patients with metastatic, castration-resistant prostate cancer. *Oncotarget* **2015**, *6*, 18192–18205. [\[CrossRef\]](#)
84. van de Loosdrecht, A.A.; van Wetering, S.; Santegoets, S.; Singh, S.K.; Eeltink, C.M.; den Hartog, Y.; Koppes, M.; Kaspers, J.; Ossenkoppele, G.J.; Kruisbeek, A.M.; et al. A novel allogeneic off-the-shelf dendritic cell vaccine for post-remission treatment of elderly patients with acute myeloid leukemia. *Cancer Immunol. Immunother.* **2018**, *67*, 1505–1518. [\[CrossRef\]](#) [\[PubMed\]](#)
85. Rodriguez, J.; Castanon, E.; Perez-Gracia, J.L.; Rodriguez, I.; Viudez, A.; Alfaro, C.; Onate, C.; Perez, G.; Rotellar, F.; Inoges, S.; et al. A randomized phase II clinical trial of dendritic cell vaccination following complete resection of colon cancer liver metastasis. *J. Immunother. Cancer* **2018**, *6*, 96. [\[CrossRef\]](#)

86. Tada, F.; Abe, M.; Hirooka, M.; Ikeda, Y.; Hiasa, Y.; Lee, Y.; Jung, N.C.; Lee, W.B.; Lee, H.S.; Bae, Y.S.; et al. Phase I/II study of immunotherapy using tumor antigen-pulsed dendritic cells in patients with hepatocellular carcinoma. *Int. J. Oncol.* **2012**, *41*, 1601–1609. [CrossRef]
87. Mansilla, M.J.; Contreras-Cardone, R.; Navarro-Barriuso, J.; Cools, N.; Berneman, Z.; Ramo-Tello, C.; Martinez-Caceres, E.M. Cryopreserved vitamin D3-tolerogenic dendritic cells pulsed with autoantigens as a potential therapy for multiple sclerosis patients. *J. Neuroinflamm.* **2016**, *13*, 113. [CrossRef]
88. Phuphanich, S.; Wheeler, C.J.; Rudnick, J.D.; Mazer, M.; Wang, H.; Nuno, M.A.; Richardson, J.E.; Fan, X.; Ji, J.; Chu, R.M.; et al. Phase I trial of a multi-epitope-pulsed dendritic cell vaccine for patients with newly diagnosed glioblastoma. *Cancer Immunol. Immunother.* **2013**, *62*, 125–135. [CrossRef]
89. Nagayama, H.; Sato, K.; Morishita, M.; Uchimar, K.; Oyaizu, N.; Inazawa, T.; Yamasaki, T.; Enomoto, M.; Nakaoka, T.; Nakamura, T.; et al. Results of a phase I clinical study using autologous tumour lysate-pulsed monocyte-derived mature dendritic cell vaccinations for stage IV malignant melanoma patients combined with low dose interleukin-2. *Melanoma Res.* **2003**, *13*, 521–530. [CrossRef]
90. Lau, R.; Wang, F.; Jeffery, G.; Marty, V.; Kuniyoshi, J.; Bade, E.; Ryback, M.E.; Weber, J. Phase I trial of intravenous peptide-pulsed dendritic cells in patients with metastatic melanoma. *J. Immunother.* **2001**, *24*, 66–78. [CrossRef]
91. Imhof, M.; Lipovac, M.; Angleitner-Boubenizek, L.; Barta, J.; Gomez, I.; Hrdina, A.; Krupa, E.; Lafleur, J.; Lang, I.; Pieta, K.; et al. Double-loaded mature dendritic cell (DC) therapy for non-HLA-restricted patients with advanced ovarian cancer: Final results of a clinical phase I study. *J. Clin. Oncol.* **2013**, *31*, 3052. [CrossRef]
92. Cobb, A.; Roberts, L.K.; Palucka, A.K.; Mead, H.; Montes, M.; Ranganathan, R.; Burkeholder, S.; Finholt, J.P.; Blankenship, D.; King, B.; et al. Development of a HIV-1 lipopeptide antigen pulsed therapeutic dendritic cell vaccine. *J. Immunol. Methods* **2011**, *365*, 27–37. [CrossRef] [PubMed]
93. Kitawaki, T.; Kadowaki, N.; Fukunaga, K.; Kasai, Y.; Maekawa, T.; Ohmori, K.; Itoh, T.; Shimizu, A.; Kuzushima, K.; Kondo, T.; et al. Cross-priming of CD8(+) T cells in vivo by dendritic cells pulsed with autologous apoptotic leukemic cells in immunotherapy for elderly patients with acute myeloid leukemia. *Exp. Hematol.* **2011**, *39*, 424–433.e2. [CrossRef] [PubMed]
94. Shinde, P.; Khan, N.; Melinkeri, S.; Kale, V.; Limaye, L. Freezing of dendritic cells with trehalose as an additive in the conventional freezing medium results in improved recovery after cryopreservation. *Transfusion* **2019**, *59*, 686–696. [CrossRef]
95. Pi, C.H.; Yu, G.; Petersen, A.; Hubel, A. Characterizing the “sweet spot” for the preservation of a T-cell line using osmolytes. *Sci. Rep.* **2018**, *8*, 16223. [CrossRef]
96. Celluzzi, C.M.; Welbon, C. A simple cryopreservation method for dendritic cells and cells used in their derivation and functional assessment. *Transfusion* **2003**, *43*, 488–494. [CrossRef]
97. Kantoff, P.W.; Higano, C.S.; Shore, N.D.; Berger, E.R.; Small, E.J.; Penson, D.F.; Redfern, C.H.; Ferrari, A.C.; Dreicer, R.; Sims, R.B.; et al. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *N. Engl. J. Med.* **2010**, *363*, 411–422. [CrossRef]
98. Patient-Specific Dendritic Cell Vaccines with Autologous Tumor Antigens in 72 Patients with Metastatic Melanoma. Available online: <https://clinicaltrials.gov/study/NCT00012064?cond=Cancer&term=Dendritic%20Cell&intr=Dendritic%20Cells&limit=100&aggFilters=status:com&rank=32&tab=results> (accessed on 1 December 2025).
99. Chang, C.N.; Huang, Y.C.; Yang, D.M.; Kikuta, K.; Wei, K.J.; Kubota, T.; Yang, W.K. A phase I/II clinical trial investigating the adverse and therapeutic effects of a postoperative autologous dendritic cell tumor vaccine in patients with malignant glioma. *J. Clin. Neurosci.* **2011**, *18*, 1048–1054. [CrossRef]
100. Cho, D.Y.; Yang, W.K.; Lee, H.C.; Hsu, D.M.; Lin, H.L.; Lin, S.Z.; Chen, C.C.; Harn, H.J.; Liu, C.L.; Lee, W.Y.; et al. Adjuvant immunotherapy with whole-cell lysate dendritic cells vaccine for glioblastoma multiforme: A phase II clinical trial. *World Neurosurg.* **2012**, *77*, 736–744. [CrossRef]
101. Ramanathan, R.; Choudry, H.; Jones, H.; Girgis, M.; Gooding, W.; Kalinski, P.; Bartlett, D.L. Phase II Trial of Adjuvant Dendritic Cell Vaccine in Combination with Celecoxib, Interferon-alpha, and Rintatolimod in Patients Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Metastases. *Ann. Surg. Oncol.* **2021**, *28*, 4637–4646. [CrossRef]
102. Geskin, L.J.; Damiano, J.J.; Patrone, C.C.; Butterfield, L.H.; Kirkwood, J.M.; Falo, L.D. Three antigen-loading methods in dendritic cell vaccines for metastatic melanoma. *Melanoma Res.* **2018**, *28*, 211–221. [CrossRef] [PubMed]
103. Florcken, A.; Kopp, J.; van Lessen, A.; Movassaghi, K.; Takvorian, A.; Johrens, K.; Mobs, M.; Schonemann, C.; Sawitzki, B.; Egerer, K.; et al. Allogeneic partially HLA-matched dendritic cells pulsed with autologous tumor cell lysate as a vaccine in metastatic renal cell cancer: A clinical phase I/II study. *Hum. Vaccin. Immunother.* **2013**, *9*, 1217–1227. [CrossRef] [PubMed]
104. Laurell, A.; Lonnemark, M.; Brekkan, E.; Magnusson, A.; Tolf, A.; Wallgren, A.C.; Andersson, B.; Adamson, L.; Kiessling, R.; Karlsson-Parra, A. Intratumorally injected pro-inflammatory allogeneic dendritic cells as immune enhancers: A first-in-human study in unfavourable risk patients with metastatic renal cell carcinoma. *J. Immunother. Cancer* **2017**, *5*, 52. [CrossRef] [PubMed]
105. Pandha, H.S.; John, R.J.; Hutchinson, J.; James, N.; Whelan, M.; Corbishley, C.; Dalglish, A.G. Dendritic cell immunotherapy for urological cancers using cryopreserved allogeneic tumour lysate-pulsed cells: A phase I/II study. *BJU Int.* **2004**, *94*, 412–418. [CrossRef]

106. Frank, M.O.; Kaufman, J.; Tian, S.; Suarez-Farinas, M.; Parveen, S.; Blachere, N.E.; Morris, M.J.; Slovin, S.; Scher, H.I.; Albert, M.L.; et al. Harnessing naturally occurring tumor immunity: A clinical vaccine trial in prostate cancer. *PLoS ONE* **2010**, *5*, e12367. [CrossRef]
107. Carpenter, E.L.; Van Decar, S.; Adams, A.M.; O'Shea, A.E.; McCarthy, P.; Chick, R.C.; Clifton, G.T.; Vreeland, T.; Valdera, F.A.; Tiwari, A.; et al. Prospective, randomized, double-blind phase 2B trial of the TLPO and TLPLDC vaccines to prevent recurrence of resected stage III/IV melanoma: A prespecified 36-month analysis. *J. Immunother. Cancer* **2023**, *11*, e006665. [CrossRef]
108. A Phase II Feasibility Study of Adjuvant Intra-Nodal Autologous Dendritic Cell Vaccination for Newly Diagnosed Glioblastoma Multiforme. Available online: <https://clinicaltrials.gov/study/NCT00323115> (accessed on 1 December 2025).
109. Fadul, C.E.; Fisher, J.L.; Hampton, T.H.; Lallana, E.C.; Li, Z.; Gui, J.; Szczepiorkowski, Z.M.; Tosteson, T.D.; Rhodes, C.H.; Wishart, H.A.; et al. Immune response in patients with newly diagnosed glioblastoma multiforme treated with intranodal autologous tumor lysate-dendritic cell vaccination after radiation chemotherapy. *J. Immunother.* **2011**, *34*, 382–389. [CrossRef]
110. Liao, L.M.; Ashkan, K.; Tran, D.D.; Campian, J.L.; Trusheim, J.E.; Cobbs, C.S.; Heth, J.A.; Salacz, M.; Taylor, S.; D'Andre, S.D.; et al. First results on survival from a large Phase 3 clinical trial of an autologous dendritic cell vaccine in newly diagnosed glioblastoma. *J. Transl. Med.* **2018**, *29*, 142. Erratum in *J. Transl. Med.* **2018**, *29*, 179. <https://doi.org/10.1186/s12967-018-1552-1>. [CrossRef]
111. Liao, L.M.; Ashkan, K.; Brem, S.; Campian, J.L.; Trusheim, J.E.; Iwamoto, F.M.; Tran, D.D.; Ansstas, G.; Cobbs, C.S.; Heth, J.A.; et al. Association of Autologous Tumor Lysate-Loaded Dendritic Cell Vaccination With Extension of Survival Among Patients With Newly Diagnosed and Recurrent Glioblastoma. *JAMA Oncol.* **2022**, *9*, 112–121. [CrossRef]
112. The Epitope-Enhanced TARP Peptide Can Induce Specific T Cells That Can Recognize Wild-Type TARP Tetramer by Either Peptide or Peptide-Pulsed DC Vaccination in Patients with Prostate Cancer. Available online: <https://clinicaltrials.gov/study/NCT00972309?cond=Cancer&term=Dendritic%20Cell&intr=Dendritic%20Cells&limit=100&aggFilters=status:com&rank=102&tab=history&a=110#version-content-panel> (accessed on 1 December 2025).
113. Berzofsky, J.A.; Wood, L.V.; Terabe, M. Cancer vaccines: 21st century approaches to harnessing an ancient modality to fight cancer. *Expert. Rev. Vaccines* **2013**, *12*, 1115–1118. [CrossRef]
114. Wood, L.V.; Fojo, A.; Roberson, B.D.; Hughes, M.S.; Dahut, W.; Gulley, J.L.; Madan, R.A.; Arlen, P.M.; Sabatino, M.; Stronck, D.F.; et al. TARP vaccination is associated with slowing in PSA velocity and decreasing tumor growth rates in patients with Stage D0 prostate cancer. *Oncoimmunology* **2016**, *5*, e1197459. [CrossRef] [PubMed]
115. Okada, H.; Kalinski, P.; Ueda, R.; Hoji, A.; Kohanbash, G.; Donegan, T.E.; Mintz, A.H.; Engh, J.A.; Bartlett, D.L.; Brown, C.K.; et al. Induction of CD8+ T-cell responses against novel glioma-associated antigen peptides and clinical activity by vaccinations with alpha-type 1 polarized dendritic cells and polyinosinic-polycytidylic acid stabilized by lysine and carboxymethylcellulose in patients with recurrent malignant glioma. *J. Clin. Oncol.* **2011**, *29*, 330–336. [CrossRef] [PubMed]
116. Sharma, A.; Koldovsky, U.; Xu, S.; Mick, R.; Roses, R.; Fitzpatrick, E.; Weinstein, S.; Nisenbaum, H.; Levine, B.L.; Fox, K.; et al. HER-2 pulsed dendritic cell vaccine can eliminate HER-2 expression and impact ductal carcinoma in situ. *Cancer* **2012**, *118*, 4354–4362. [CrossRef] [PubMed]
117. Maeng, H.M.; Moore, B.N.; Bagheri, H.; Steinberg, S.M.; Inglefield, J.; Dunham, K.; Wei, W.Z.; Morris, J.C.; Terabe, M.; England, L.C.; et al. Phase I Clinical Trial of an Autologous Dendritic Cell Vaccine Against HER2 Shows Safety and Preliminary Clinical Efficacy. *Front. Oncol.* **2021**, *11*, 789078. [CrossRef]
118. Wen, P.Y.; Reardon, D.A.; Armstrong, T.S.; Phuphanich, S.; Aiken, R.D.; Landolfi, J.C.; Curry, W.T.; Zhu, J.J.; Glantz, M.; Peereboom, D.M.; et al. A Randomized Double-Blind Placebo-Controlled Phase II Trial of Dendritic Cell Vaccine ICT-107 in Newly Diagnosed Patients with Glioblastoma. *Clin. Cancer Res.* **2019**, *25*, 5799–5807. [CrossRef]
119. Hirschowitz, E.A.; Foody, T.; Kryscio, R.; Dickson, L.; Sturgill, J.; Yannelli, J. Autologous dendritic cell vaccines for non-small-cell lung cancer. *J. Clin. Oncol.* **2004**, *22*, 2808–2815. [CrossRef]
120. Morse, M.A.; Niedzwiecki, D.; Marshall, J.L.; Garrett, C.; Chang, D.Z.; Aklilu, M.; Crocenzi, T.S.; Cole, D.J.; Dessureault, S.; Hobeika, A.C.; et al. A randomized phase II study of immunization with dendritic cells modified with poxvectors encoding CEA and MUC1 compared with the same poxvectors plus GM-CSF for resected metastatic colorectal cancer. *Ann. Surg.* **2013**, *258*, 879–886. [CrossRef]
121. Gray, H.J.; Benigno, B.; Berek, J.; Chang, J.; Mason, J.; Mileskin, L.; Mitchell, P.; Moradi, M.; Recio, F.O.; Michener, C.M.; et al. Progression-free and overall survival in ovarian cancer patients treated with CVac, a mucin 1 dendritic cell therapy in a randomized phase 2 trial. *J. Immunother. Cancer* **2016**, *4*, 34. [CrossRef]
122. Chiappori, A.A.; Williams, C.C.; Gray, J.E.; Tanvetyanon, T.; Haura, E.B.; Creelan, B.C.; Thapa, R.; Chen, D.T.; Simon, G.R.; Bepler, G.; et al. Randomized-controlled phase II trial of salvage chemotherapy after immunization with a TP53-transfected dendritic cell-based vaccine (Ad.p53-DC) in patients with recurrent small cell lung cancer. *Cancer Immunol. Immunother.* **2019**, *68*, 517–527. [CrossRef]
123. Soliman, H.; Khambati, F.; Han, H.S.; Ismail-Khan, R.; Bui, M.M.; Sullivan, D.M.; Antonia, S. A phase-1/2 study of adenovirus-p53 transduced dendritic cell vaccine in combination with indoximod in metastatic solid tumors and invasive breast cancer. *Oncotarget* **2018**, *9*, 10110–10117. [CrossRef]

124. Kongsted, P.; Ellebæk, E.; Borch, T.H.; Iversen, T.Z.; Andersen, R.; Met, Ö.; Hansen, M.; Sengeløv, L.; Svane, I.M. Dendritic cell vaccination in combination with docetaxel for patients with prostate cancer – a randomized phase II study. *Ann. Oncol.* **2016**, *27*, vi371. [\[CrossRef\]](#)
125. Kongsted, P.; Borch, T.H.; Ellebaek, E.; Iversen, T.Z.; Andersen, R.; Met, O.; Hansen, M.; Lindberg, H.; Sengelov, L.; Svane, I.M. Dendritic cell vaccination in combination with docetaxel for patients with metastatic castration-resistant prostate cancer: A randomized phase II study. *Cytotherapy* **2017**, *19*, 500–513. [\[CrossRef\]](#) [\[PubMed\]](#)
126. Storkus, W.J.; Maurer, D.; Lin, Y.; Ding, F.; Bose, A.; Lowe, D.; Rose, A.; DeMark, M.; Karapetyan, L.; Taylor, J.L.; et al. Dendritic cell vaccines targeting tumor blood vessel antigens in combination with dasatinib induce therapeutic immune responses in patients with checkpoint-refractory advanced melanoma. *J. Immunother. Cancer* **2021**, *9*, e003675. [\[CrossRef\]](#) [\[PubMed\]](#)
127. Raj, S.; Bui, M.M.; Springett, G.; Conley, A.; Lavilla-Alonso, S.; Zhao, X.; Chen, D.; Haysek, R.; Gonzalez, R.; Letson, G.D.; et al. Long-Term Clinical Responses of Neoadjuvant Dendritic Cell Infusions and Radiation in Soft Tissue Sarcoma. *Sarcoma* **2015**, *2015*, 614736. [\[CrossRef\]](#) [\[PubMed\]](#)
128. Younis, A.; Gribben, J. Immune Checkpoint Inhibitors: Fundamental Mechanisms, Current Status and Future Directions. *Immuno* **2024**, *4*, 186–210. [\[CrossRef\]](#)
129. Reardon, D.A.; Brandes, A.A.; Omuro, A.; Mulholland, P.; Lim, M.; Wick, A.; Baehring, J.; Ahluwalia, M.S.; Roth, P.; Bahr, O.; et al. Effect of Nivolumab vs Bevacizumab in Patients with Recurrent Glioblastoma: The CheckMate 143 Phase 3 Randomized Clinical Trial. *JAMA Oncol.* **2020**, *6*, 1003–1010. [\[CrossRef\]](#)
130. Omuro, A.; Brandes, A.A.; Carpentier, A.F.; Idbaih, A.; Reardon, D.A.; Cloughesy, T.; Sumrall, A.; Baehring, J.; van den Bent, M.; Bahr, O.; et al. Radiotherapy combined with nivolumab or temozolomide for newly diagnosed glioblastoma with unmethylated MGMT promoter: An international randomized phase III trial. *Neuro Oncol.* **2023**, *25*, 123–134. [\[CrossRef\]](#)
131. Lim, M.; Weller, M.; Idbaih, A.; Steinbach, J.; Finocchiaro, G.; Raval, R.R.; Ansstas, G.; Baehring, J.; Taylor, J.W.; Honnorat, J.; et al. Phase III trial of chemoradiotherapy with temozolomide plus nivolumab or placebo for newly diagnosed glioblastoma with methylated MGMT promoter. *Neuro Oncol.* **2022**, *24*, 1935–1949. [\[CrossRef\]](#)
132. Henriksen, A.; Dyhl-Polk, A.; Chen, I.; Nielsen, D. Checkpoint inhibitors in pancreatic cancer. *Cancer Treat. Rev.* **2019**, *78*, 17–30. [\[CrossRef\]](#)
133. Lim, S.Y.; Shklovskaya, E.; Lee, J.H.; Pedersen, B.; Stewart, A.; Ming, Z.; Irvine, M.; Shivalingam, B.; Saw, R.P.M.; Menzies, A.M.; et al. The molecular and functional landscape of resistance to immune checkpoint blockade in melanoma. *Nat. Commun.* **2023**, *14*, 1516. [\[CrossRef\]](#)
134. Prasad, V.; Haslam, A.; Olivier, T. Updated estimates of eligibility and response: Immune checkpoint inhibitors. *J. Clin. Oncol.* **2024**, *42*, e14613. [\[CrossRef\]](#)
135. Wang, Y.; Guo, Y.; Tan, A.C.; Zhao, L.; Shi, X.; Chen, Y.; Sun, R.C.; Liu, M.; Su, J.; George, T.J.; et al. A real-world cohort study of immune-related adverse events in patients receiving immune checkpoint inhibitors. *npj Precis. Oncol.* **2025**, *9*, 346. [\[CrossRef\]](#) [\[PubMed\]](#)
136. Dohnal, A.M.; Witt, V.; Hugel, H.; Holter, W.; Gadner, H.; Felzmann, T. Phase I study of tumor Ag-loaded IL-12 secreting semi-mature DC for the treatment of pediatric cancer. *Cytotherapy* **2007**, *9*, 755–770. [\[CrossRef\]](#) [\[PubMed\]](#)
137. Chung, D.J.; Shah, N.; Wu, J.; Logan, B.; Bisharat, L.; Callander, N.; Cheloni, G.; Anderson, K.; Chodon, T.; Dhakal, B.; et al. Randomized Phase II Trial of Dendritic Cell/Myeloma Fusion Vaccine with Lenalidomide Maintenance after Upfront Autologous Hematopoietic Cell Transplantation for Multiple Myeloma: BMT CTN 1401. *Clin. Cancer Res.* **2023**, *29*, 4784–4796. [\[CrossRef\]](#)
138. Chung, D.J.; Shah, N.; Wu, J.; Logan, B.; Bisharat, L.; Callander, N.; Cheloni, G.; Anderson, K.; Chodon, T.; Dhakal, B.; et al. Correction: Randomized Phase II Trial of Dendritic Cell/Myeloma Fusion Vaccine with Lenalidomide Maintenance after Upfront Autologous Hematopoietic Cell Transplantation for Multiple Myeloma: BMT CTN 1401. *Clin. Cancer Res.* **2024**, *30*, 4542. [\[CrossRef\]](#)
139. Mackall, C.L.; Rhee, E.H.; Read, E.J.; Khuu, H.M.; Leitman, S.F.; Bernstein, D.; Tesso, M.; Long, L.M.; Grindler, D.; Merino, M.; et al. A pilot study of consolidative immunotherapy in patients with high-risk pediatric sarcomas. *Clin. Cancer Res.* **2008**, *14*, 4850–4858. [\[CrossRef\]](#)
140. Herbert, G.S.; Vreeland, T.J.; Clifton, G.T.; Greene, J.M.; Jackson, D.O.; Hardin, M.O.; Hale, D.F.; Berry, J.S.; Nichol, P.; Yin, S.; et al. Initial phase I/IIa trial results of an autologous tumor lysate, particle-loaded, dendritic cell (TLPLDC) vaccine in patients with solid tumors. *Vaccine* **2018**, *36*, 3247–3253. [\[CrossRef\]](#)
141. Plesca, I.; Benesova, I.; Beer, C.; Sommer, U.; Muller, L.; Wehner, R.; Heiduk, M.; Aust, D.; Baretton, G.; Bachmann, M.P.; et al. Clinical Significance of Tumor-Infiltrating Conventional and Plasmacytoid Dendritic Cells in Pancreatic Ductal Adenocarcinoma. *Cancers* **2022**, *1*, 1216. [\[CrossRef\]](#)
142. Aspod, C.; Leccia, M.T.; Charles, J.; Plumas, J. Plasmacytoid dendritic cells support melanoma progression by promoting Th2 and regulatory immunity through OX40L and ICOSL. *Cancer Immunol. Res.* **2013**, *1*, 402–415. [\[CrossRef\]](#)

143. Labidi-Galy, S.I.; Treilleux, I.; Goddard-Leon, S.; Combes, J.D.; Blay, J.Y.; Ray-Coquard, I.; Caux, C.; Bendriss-Vermare, N. Plasmacytoid dendritic cells infiltrating ovarian cancer are associated with poor prognosis. *Oncoimmunology* **2012**, *1*, 380–382. [\[CrossRef\]](#)
144. Pang, L.; Ng, K.T.; Liu, J.; Yeung, W.O.; Zhu, J.; Chiu, T.S.; Liu, H.; Chen, Z.; Lo, C.M.; Man, K. Plasmacytoid dendritic cells recruited by HIF-1 α /eADO/ADORA1 signaling induce immunosuppression in hepatocellular carcinoma. *Cancer Lett.* **2021**, *522*, 80–92. [\[CrossRef\]](#)
145. Treilleux, I.; Blay, J.Y.; Bendriss-Vermare, N.; Ray-Coquard, I.; Bachelot, T.; Guastalla, J.P.; Bremond, A.; Goddard, S.; Pin, J.J.; Barthelemy-Dubois, C.; et al. Dendritic cell infiltration and prognosis of early stage breast cancer. *Clin. Cancer Res.* **2004**, *10*, 7466–7474. [\[CrossRef\]](#) [\[PubMed\]](#)
146. Han, Y.; Liu, S.M.; Jin, R.; Meng, W.; Wu, Y.L.; Li, H. A risk score combining co-expression modules related to myeloid cells and alternative splicing associates with response to PD-1/PD-L1 blockade in non-small cell lung cancer. *Front. Immunol.* **2023**, *14*, 1178193. [\[CrossRef\]](#) [\[PubMed\]](#)
147. Ding, S.; Qiao, N.; Zhu, Q.; Tong, Y.; Wang, S.; Chen, X.; Tian, Q.; Xiao, Y.; Shen, K. Single-cell atlas reveals a distinct immune profile fostered by T cell-B cell crosstalk in triple negative breast cancer. *Cancer Commun.* **2023**, *43*, 661–684. [\[CrossRef\]](#)
148. Yin, X.K.; Wang, C.; Feng, L.L.; Bai, S.M.; Feng, W.X.; Ouyang, N.T.; Chu, Z.H.; Fan, X.J.; Qin, Q.Y. Expression Pattern and Prognostic Value of CTLA-4, CD86, and Tumor-Infiltrating Lymphocytes in Rectal Cancer after Neoadjuvant Chemo(radio)therapy. *Cancers* **2022**, *14*, 5573. [\[CrossRef\]](#)
149. Pellegatta, S.; Eoli, M.; Cuccarini, V.; Anghileri, E.; Pollo, B.; Pessina, S.; Frigerio, S.; Servida, M.; Cuppini, L.; Antozzi, C.; et al. Survival gain in glioblastoma patients treated with dendritic cell immunotherapy is associated with increased NK but not CD8+ T cell activation in the presence of adjuvant temozolomide. *Oncoimmunology* **2018**, *7*, e1412901. [\[CrossRef\]](#) [\[PubMed\]](#)
150. Slingluff, C.L., Jr.; Petroni, G.R.; Yamshchikov, G.V.; Barnd, D.L.; Eastham, S.; Galavotti, H.; Patterson, J.W.; Deacon, D.H.; Hibbitts, S.; Teates, D.; et al. Clinical and immunologic results of a randomized phase II trial of vaccination using four melanoma peptides either administered in granulocyte-macrophage colony-stimulating factor in adjuvant or pulsed on dendritic cells. *J. Clin. Oncol.* **2003**, *21*, 4016–4026. [\[CrossRef\]](#)
151. Bhardwaj, N.; Friedlander, P.A.; Pavlick, A.C.; Ernstoff, M.S.; Gastman, B.R.; Hanks, B.A.; Curti, B.D.; Albertini, M.R.; Luke, J.J.; Blazquez, A.B.; et al. Flt3 ligand augments immune responses to anti-DEC-205-NY-ESO-1 vaccine through expansion of dendritic cell subsets. *Nat. Cancer* **2020**, *1*, 1204–1217. [\[CrossRef\]](#)
152. Maraskovsky, E.; Brasel, K.; Teepe, M.; Roux, E.R.; Lyman, S.D.; Shortman, K.; McKenna, H.J. Dramatic increase in the numbers of functionally mature dendritic cells in Flt3 ligand-treated mice: Multiple dendritic cell subpopulations identified. *J. Exp. Med.* **1996**, *184*, 1953–1962. [\[CrossRef\]](#)
153. Karsunky, H.; Merad, M.; Cozzio, A.; Weissman, I.L.; Manz, M.G. Flt3 ligand regulates dendritic cell development from Flt3+ lymphoid and myeloid-committed progenitors to Flt3+ dendritic cells in vivo. *J. Exp. Med.* **2003**, *198*, 305–313. [\[CrossRef\]](#)
154. Bonehill, A.; Van Nuffel, A.M.; Corthals, J.; Tuyaeerts, S.; Heirman, C.; Francois, V.; Colau, D.; van der Bruggen, P.; Neyns, B.; Thielemans, K. Single-step antigen loading and activation of dendritic cells by mRNA electroporation for the purpose of therapeutic vaccination in melanoma patients. *Clin. Cancer Res.* **2009**, *15*, 3366–3375. [\[CrossRef\]](#)
155. Ghasemi, A.; Martinez-Usatorre, A.; Liu, Y.; Demagny, H.; Li, L.; Mohammadzadeh, Y.; Hurtado, A.; Hicham, M.; Henneman, L.; Pritchard, C.E.J.; et al. Dendritic cell progenitors engineered to express extracellular-vesicle–internalizing receptors enhance cancer immunotherapy in mouse models. *Nat. Commun.* **2025**, *16*, 9148. [\[CrossRef\]](#)
156. Perroud, M.W., Jr.; Honma, H.N.; Barbeiro, A.S.; Gilli, S.C.; Almeida, M.T.; Vassallo, J.; Saad, S.T.; Zambon, L. Mature autologous dendritic cell vaccines in advanced non-small cell lung cancer: A phase I pilot study. *J. Exp. Clin. Cancer Res.* **2011**, *30*, 65. [\[CrossRef\]](#)
157. Amin, A.; Dudek, A.Z.; Logan, T.F.; Lance, R.S.; Holzbeierlein, J.M.; Knox, J.J.; Master, V.A.; Pal, S.K.; Miller, W.H., Jr.; Karsh, L.I.; et al. Survival with AGS-003, an autologous dendritic cell-based immunotherapy, in combination with sunitinib in unfavorable risk patients with advanced renal cell carcinoma (RCC): Phase 2 study results. *J. Immunother. Cancer* **2015**, *3*, 14. [\[CrossRef\]](#)
158. Avigan, D.E.; Vasir, B.; George, D.J.; Oh, W.K.; Atkins, M.B.; McDermott, D.F.; Kantoff, P.W.; Figlin, R.A.; Vasconcelles, M.J.; Xu, Y.; et al. Phase I/II study of vaccination with electrofused allogeneic dendritic cells/autologous tumor-derived cells in patients with stage IV renal cell carcinoma. *J. Immunother.* **2007**, *30*, 749–761. [\[CrossRef\]](#)
159. Marten, A.; Renoth, S.; Heinicke, T.; Albers, P.; Pauli, A.; Mey, U.; Caspari, R.; Flieger, D.; Hanfland, P.; Von Ruecker, A.; et al. Allogeneic dendritic cells fused with tumor cells: Preclinical results and outcome of a clinical phase I/II trial in patients with metastatic renal cell carcinoma. *Hum. Gene Ther.* **2003**, *14*, 483–494. [\[CrossRef\]](#)
160. Rob, L.; Cibula, D.; Knapp, P.; Mallmann, P.; Klat, J.; Minar, L.; Bartos, P.; Chovanec, J.; Valha, P.; Pluta, M.; et al. Safety and efficacy of dendritic cell-based immunotherapy DCVAC/OvCa added to first-line chemotherapy (carboplatin plus paclitaxel) for epithelial ovarian cancer: A phase 2, open-label, multicenter, randomized trial. *J. Immunother. Cancer* **2022**, *10*, e003190. [\[CrossRef\]](#)

161. Koenenman, B.; Schreibelt, G.; Duiveman-de Boer, T.; Bos, K.; van Oorschot, T.; Pots, J.; Scharenborg, N.; de Boer, A.; Hins-de Bree, S.; de Haas, N.; et al. NEOadjuvant Dendritic cell therapy added to first line standard of care in advanced epithelial Ovarian Cancer (NEODOC): Protocol of a first-in-human, exploratory, single-centre phase I/II trial in the Netherlands. *BMJ Open* **2025**, *15*, e102184. [\[CrossRef\]](#)
162. Koenenman, B.J.; Schreibelt, G.; Gorris, M.A.J.; Hins-de Bree, S.; Westdorp, H.; Ottevanger, P.B.; de Vries, I.J.M. Dendritic cell vaccination combined with carboplatin/paclitaxel for metastatic endometrial cancer patients: Results of a phase I/II trial. *Front. Immunol.* **2024**, *15*, 1368103. [\[CrossRef\]](#)
163. Buchroithner, J.; Erhart, F.; Pichler, J.; Widhalm, G.; Preusser, M.; Stockhammer, G.; Nowosielski, M.; Iglseder, S.; Freyschlag, C.F.; Oberndorfer, S.; et al. Audencel Immunotherapy Based on Dendritic Cells Has No Effect on Overall and Progression-Free Survival in Newly Diagnosed Glioblastoma: A Phase II Randomized Trial. *Cancers* **2018**, *10*, 372. [\[CrossRef\]](#)
164. Cibula, D.; Rob, L.; Mallmann, P.; Knapp, P.; Klat, J.; Chovanec, J.; Minar, L.; Melichar, B.; Hein, A.; Kieszko, D.; et al. Dendritic cell-based immunotherapy (DCVAC/OvCa) combined with second-line chemotherapy in platinum-sensitive ovarian cancer (SOV02): A randomized, open-label, phase 2 trial. *Gynecol. Oncol.* **2021**, *162*, 652–660. [\[CrossRef\]](#)
165. Baek, S.; Kim, C.S.; Kim, S.B.; Kim, Y.M.; Kwon, S.W.; Kim, Y.; Kim, H.; Lee, H. Combination therapy of renal cell carcinoma or breast cancer patients with dendritic cell vaccine and IL-2: Results from a phase I/II trial. *J. Transl. Med.* **2011**, *9*, 178. [\[CrossRef\]](#)
166. Schuler, P.J.; Harasymczuk, M.; Visus, C.; Deleo, A.; Trivedi, S.; Lei, Y.; Argiris, A.; Gooding, W.; Butterfield, L.H.; Whiteside, T.L.; et al. Phase I dendritic cell p53 peptide vaccine for head and neck cancer. *Clin. Cancer Res.* **2014**, *20*, 2433–2444. [\[CrossRef\]](#)
167. Thomsen, L.C.V.; Honore, A.; Reisaeter, L.A.R.; Almas, B.; Borretzen, A.; Helle, S.I.; Forde, K.; Kristoffersen, E.K.; Kaada, S.H.; Melve, G.K.; et al. A phase I prospective, non-randomized trial of autologous dendritic cell-based cryoimmunotherapy in patients with metastatic castration-resistant prostate cancer. *Cancer Immunol. Immunother.* **2023**, *72*, 2357–2373. [\[CrossRef\]](#)
168. Akiyama, Y.; Oshita, C.; Kume, A.; Iizuka, A.; Miyata, H.; Komiyama, M.; Ashizawa, T.; Yagoto, M.; Abe, Y.; Mitsuya, K.; et al. alpha-type-1 polarized dendritic cell-based vaccination in recurrent high-grade glioma: A phase I clinical trial. *BMC Cancer* **2012**, *12*, 623. [\[CrossRef\]](#)
169. Bota, D.A.; Piccioni, D.E.; Duma, C.M.; Kesari, S.; Carrillo, J.A.; LaRocca, R.V.; Aiken, R.D.; Taylor, T.H.; Abedi, M.; Robles, R.M.; et al. Phase 2 trial of personal dendritic cell vaccines in newly diagnosed glioblastoma: 3-year follow-up and correlations with survival. *Hum. Vaccin. Immunother.* **2025**, *21*, 2556591. [\[CrossRef\]](#)
170. Caballero-Banos, M.; Benitez-Ribas, D.; Tabera, J.; Varea, S.; Vilana, R.; Bianchi, L.; Ayuso, J.R.; Pages, M.; Carrera, G.; Cuatrecasas, M.; et al. Phase II randomised trial of autologous tumour lysate dendritic cell plus best supportive care compared with best supportive care in pre-treated advanced colorectal cancer patients. *Eur. J. Cancer* **2016**, *64*, 167–174. [\[CrossRef\]](#)
171. Mitsuya, K.; Akiyama, Y.; Iizuka, A.; Miyata, H.; Deguchi, S.; Hayashi, N.; Maeda, C.; Kondou, R.; Kanematsu, A.; Watanabe, K.; et al. Alpha-type-1 Polarized Dendritic Cell-based Vaccination in Newly Diagnosed High-grade Glioma: A Phase II Clinical Trial. *Anticancer. Res.* **2020**, *40*, 6473–6484. [\[CrossRef\]](#)
172. Oshita, C.; Takikawa, M.; Kume, A.; Miyata, H.; Ashizawa, T.; Iizuka, A.; Kiyohara, Y.; Yoshikawa, S.; Tanosaki, R.; Yamazaki, N.; et al. Dendritic cell-based vaccination in metastatic melanoma patients: Phase II clinical trial. *Oncol. Rep.* **2012**, *28*, 1131–1138. [\[CrossRef\]](#)
173. Wilgenhof, S.; Van Nuffel, A.M.T.; Benteyn, D.; Corthals, J.; Aerts, C.; Heirman, C.; Van Riet, I.; Bonehill, A.; Thielemans, K.; Neyns, B. A phase IB study on intravenous synthetic mRNA electroporated dendritic cell immunotherapy in pretreated advanced melanoma patients. *Ann. Oncol.* **2013**, *24*, 2686–2693. [\[CrossRef\]](#)
174. Matsui, H.; Hazama, S.; Nakajima, M.; Xu, M.; Matsukuma, S.; Tokumitsu, Y.; Shindo, Y.; Tomochika, S.; Yoshida, S.; Iida, M.; et al. Correction to: Novel adjuvant dendritic cell therapy with transfection of heat-shock protein 70 messenger RNA for patients with hepatocellular carcinoma: A phase I/II prospective randomized controlled clinical trial. *Cancer Immunol. Immunother.* **2021**, *70*, 959. [\[CrossRef\]](#) [\[PubMed\]](#)
175. Ellebaek, E.; Engell-Noerregaard, L.; Iversen, T.Z.; Froesig, T.M.; Munir, S.; Hadrup, S.R.; Andersen, M.H.; Svane, I.M. Metastatic melanoma patients treated with dendritic cell vaccination, Interleukin-2 and metronomic cyclophosphamide: Results from a phase II trial. *Cancer Immunol. Immunother.* **2012**, *61*, 1791–1804. [\[CrossRef\]](#) [\[PubMed\]](#)
176. Inoges, S.; Tejada, S.; de Cerio, A.L.; Gallego Perez-Larraya, J.; Espinos, J.; Idoate, M.A.; Dominguez, P.D.; de Eulate, R.G.; Aristu, J.; Bendandi, M.; et al. A phase II trial of autologous dendritic cell vaccination and radiochemotherapy following fluorescence-guided surgery in newly diagnosed glioblastoma patients. *J. Transl. Med.* **2017**, *15*, 104. [\[CrossRef\]](#) [\[PubMed\]](#)
177. Ishikawa, A.; Motohashi, S.; Ishikawa, E.; Fuchida, H.; Higashino, K.; Otsuji, M.; Iizasa, T.; Nakayama, T.; Taniguchi, M.; Fujisawa, T. A phase I study of alpha-galactosylceramide (KRN7000)-pulsed dendritic cells in patients with advanced and recurrent non-small cell lung cancer. *Clin. Cancer Res.* **2005**, *11*, 1910–1917. [\[CrossRef\]](#)
178. Iwashita, Y.; Tahara, K.; Goto, S.; Sasaki, A.; Kai, S.; Seike, M.; Chen, C.L.; Kawano, K.; Kitano, S. A phase I study of autologous dendritic cell-based immunotherapy for patients with unresectable primary liver cancer. *Cancer Immunol. Immunother.* **2003**, *52*, 155–161. [\[CrossRef\]](#)

179. Jacobs, J.F.; Punt, C.J.; Lesterhuis, W.J.; Suttmuller, R.P.; Brouwer, H.M.; Scharenborg, N.M.; Klasen, I.S.; Hilbrands, L.B.; Figdor, C.G.; de Vries, I.J.; et al. Dendritic cell vaccination in combination with anti-CD25 monoclonal antibody treatment: A phase I/II study in metastatic melanoma patients. *Clin. Cancer Res.* **2010**, *16*, 5067–5078. [\[CrossRef\]](#)
180. Jung, S.H.; Lee, H.J.; Lee, Y.K.; Yang, D.H.; Kim, H.J.; Rhee, J.H.; Emmrich, F.; Lee, J.J. A phase I clinical study of autologous dendritic cell therapy in patients with relapsed or refractory multiple myeloma. *Oncotarget* **2017**, *8*, 41538–41548. [\[CrossRef\]](#)
181. Kim, J.H.; Lee, Y.; Bae, Y.S.; Kim, W.S.; Kim, K.; Im, H.Y.; Kang, W.K.; Park, K.; Choi, H.Y.; Lee, H.M.; et al. Phase I/II study of immunotherapy using autologous tumor lysate-pulsed dendritic cells in patients with metastatic renal cell carcinoma. *Clin. Immunol.* **2007**, *125*, 257–267. [\[CrossRef\]](#)
182. Krishnadas, D.K.; Shusterman, S.; Bai, F.; Diller, L.; Sullivan, J.E.; Cheerva, A.C.; George, R.E.; Lucas, K.G. A phase I trial combining decitabine/dendritic cell vaccine targeting MAGE-A1, MAGE-A3 and NY-ESO-1 for children with relapsed or therapy-refractory neuroblastoma and sarcoma. *Cancer Immunol. Immunother.* **2015**, *64*, 1251–1260. [\[CrossRef\]](#)
183. Kuwabara, K.; Nishishita, T.; Morishita, M.; Oyaizu, N.; Yamashita, S.; Kanematsu, T.; Obara, T.; Mimura, Y.; Inoue, Y.; Kaminishi, M.; et al. Results of a phase I clinical study using dendritic cell vaccinations for thyroid cancer. *Thyroid* **2007**, *17*, 53–58. [\[CrossRef\]](#)
184. Lepisto, A.J.; Moser, A.J.; Zeh, H.; Lee, K.; Bartlett, D.; McKolanis, J.R.; Geller, B.A.; Schmotzer, A.; Potter, D.P.; Whiteside, T.; et al. A phase I/II study of a MUC1 peptide pulsed autologous dendritic cell vaccine as adjuvant therapy in patients with resected pancreatic and biliary tumors. *Cancer Ther.* **2008**, *6*, 955–964. [\[PubMed\]](#)
185. Loveland, B.E.; Zhao, A.; White, S.; Gan, H.; Hamilton, K.; Xing, P.X.; Pietersz, G.A.; Apostolopoulos, V.; Vaughan, H.; Karanikas, V.; et al. Mannan-MUC1-pulsed dendritic cell immunotherapy: A phase I trial in patients with adenocarcinoma. *Clin. Cancer Res.* **2006**, *12*, 869–877. [\[CrossRef\]](#) [\[PubMed\]](#)
186. Marten, A.; Flieger, D.; Renoth, S.; Weineck, S.; Albers, P.; Compes, M.; Schottker, B.; Ziske, C.; Engelhart, S.; Hanfland, P.; et al. Therapeutic vaccination against metastatic renal cell carcinoma by autologous dendritic cells: Preclinical results and outcome of a first clinical phase I/II trial. *Cancer Immunol. Immunother.* **2002**, *51*, 637–644. [\[CrossRef\]](#) [\[PubMed\]](#)
187. Marten, A.; Sievers, E.; Albers, P.; Muller, S.; Franchy, C.; von Ruecker, A.; Strunk, H.; Schild, H.H.; Schmiedel, A.; Sommer, T.; et al. Telomerase-pulsed dendritic cells: Preclinical results and outcome of a clinical phase I/II trial in patients with metastatic renal cell carcinoma. *Ger. Med. Sci.* **2006**, *4*, Doc02.
188. Mayanagi, S.; Kitago, M.; Sakurai, T.; Matsuda, T.; Fujita, T.; Higuchi, H.; Taguchi, J.; Takeuchi, H.; Itano, O.; Aiura, K.; et al. Phase I pilot study of Wilms tumor gene 1 peptide-pulsed dendritic cell vaccination combined with gemcitabine in pancreatic cancer. *Cancer Sci.* **2015**, *106*, 397–406. [\[CrossRef\]](#)
189. Mitchell, P.L.; Quinn, M.A.; Grant, P.T.; Allen, D.G.; Jobling, T.W.; White, S.C.; Zhao, A.; Karanikas, V.; Vaughan, H.; Pietersz, G.; et al. A phase 2, single-arm study of an autologous dendritic cell treatment against mucin 1 in patients with advanced epithelial ovarian cancer. *J. Immunother. Cancer* **2014**, *2*, 16. [\[CrossRef\]](#)
190. Murphy, G.; Tjoa, B.; Ragde, H.; Kenny, G.; Boynton, A. Phase I clinical trial: T-cell therapy for prostate cancer using autologous dendritic cells pulsed with HLA-A0201-specific peptides from prostate-specific membrane antigen. *Prostate* **1996**, *29*, 371–380. [\[CrossRef\]](#)
191. Nagai, K.; Adachi, T.; Harada, H.; Eguchi, S.; Sugiyama, H.; Miyazaki, Y. Dendritic Cell-based Immunotherapy Pulsed with Wilms Tumor 1 Peptide and Mucin 1 as an Adjuvant Therapy for Pancreatic Ductal Adenocarcinoma After Curative Resection: A Phase I/IIa Clinical Trial. *Anticancer. Res.* **2020**, *40*, 5765–5776. [\[CrossRef\]](#)
192. O'Rourke, M.G.; Johnson, M.; Lanagan, C.; See, J.; Yang, J.; Bell, J.R.; Slater, G.J.; Kerr, B.M.; Crowe, B.; Purdie, D.M.; et al. Durable complete clinical responses in a phase I/II trial using an autologous melanoma cell/dendritic cell vaccine. *Cancer Immunol. Immunother.* **2003**, *52*, 387–395. [\[CrossRef\]](#)
193. Ogasawara, M.; Miyashita, M.; Yamagishi, Y.; Ota, S. Phase I/II Pilot Study of Wilms' Tumor 1 Peptide-Pulsed Dendritic Cell Vaccination Combined with Conventional Chemotherapy in Patients with Head and Neck Cancer. *Ther. Apher. Dial.* **2019**, *23*, 279–288. [\[CrossRef\]](#)
194. Oosterwijk-Wakka, J.C.; Tiemessen, D.M.; Bleumer, I.; de Vries, I.J.; Jongmans, W.; Adema, G.J.; Debruyne, F.M.; de Mulder, P.H.; Oosterwijk, E.; Mulders, P.F. Vaccination of patients with metastatic renal cell carcinoma with autologous dendritic cells pulsed with autologous tumor antigens in combination with interleukin-2: A phase 1 study. *J. Immunother.* **2002**, *25*, 500–508. [\[CrossRef\]](#)
195. Ribas, A.; Camacho, L.H.; Lee, S.M.; Hersh, E.M.; Brown, C.K.; Richards, J.M.; Rodriguez, M.J.; Prieto, V.G.; Glaspy, J.A.; Oseguera, D.K.; et al. Multicenter phase II study of matured dendritic cells pulsed with melanoma cell line lysates in patients with advanced melanoma. *J. Transl. Med.* **2010**, *8*, 89. [\[CrossRef\]](#)
196. Sakakibara, M.; Kanto, T.; Hayakawa, M.; Kuroda, S.; Miyatake, H.; Itose, I.; Miyazaki, M.; Kakita, N.; Higashitani, K.; Matsubara, T.; et al. Comprehensive immunological analyses of colorectal cancer patients in the phase I/II study of quickly matured dendritic cell vaccine pulsed with carcinoembryonic antigen peptide. *Cancer Immunol. Immunother.* **2011**, *60*, 1565–1575. [\[CrossRef\]](#)
197. Santin, A.D.; Bellone, S.; Palmieri, M.; Zanolini, A.; Ravaggi, A.; Siegel, E.R.; Roman, J.J.; Pecorelli, S.; Cannon, M.J. Human papillomavirus type 16 and 18 E7-pulsed dendritic cell vaccination of stage IB or IIA cervical cancer patients: A phase I escalating-dose trial. *J. Virol.* **2008**, *82*, 1968–1979. [\[CrossRef\]](#) [\[PubMed\]](#)

198. Van Decar, S.G.; Carpenter, E.L.; Adams, A.M.; Chick, R.C.; Clifton, G.T.; Stojadinovic, A.; Vreeland, T.J.; Valdera, F.A.; Tiwari, A.; O'Shea, A.E.; et al. Tumor lysate particle only vaccine (TLPO) vs. Tumor lysate particle-loaded, dendritic cell vaccine (TLPLDC) to prevent recurrence in resected stage III/IV melanoma patients: Results of a phase I/IIa trial. *Cancer Treat. Res. Commun.* **2024**, *41*, 100843. [[CrossRef](#)] [[PubMed](#)]
199. Walker, D.G.; Laherty, R.; Tomlinson, F.H.; Chuah, T.; Schmidt, C. Results of a phase I dendritic cell vaccine trial for malignant astrocytoma: Potential interaction with adjuvant chemotherapy. *J. Clin. Neurosci.* **2008**, *15*, 114–121. [[CrossRef](#)] [[PubMed](#)]
200. Yamanaka, R.; Homma, J.; Yajima, N.; Tsuchiya, N.; Sano, M.; Kobayashi, T.; Yoshida, S.; Abe, T.; Narita, M.; Takahashi, M.; et al. Clinical evaluation of dendritic cell vaccination for patients with recurrent glioma: Results of a clinical phase I/II trial. *Clin. Cancer Res.* **2005**, *11*, 4160–4167. [[CrossRef](#)]
201. Yanagisawa, R.; Koizumi, T.; Koya, T.; Sano, K.; Koido, S.; Nagai, K.; Kobayashi, M.; Okamoto, M.; Sugiyama, H.; Shimodaira, S. WT1-pulsed Dendritic Cell Vaccine Combined with Chemotherapy for Resected Pancreatic Cancer in a Phase I Study. *Anticancer. Res.* **2018**, *38*, 2217–2225. [[CrossRef](#)]
202. Yao, Y.; Luo, F.; Tang, C.; Chen, D.; Qin, Z.; Hua, W.; Xu, M.; Zhong, P.; Yu, S.; Chen, D.; et al. Molecular subgroups and B7-H4 expression levels predict responses to dendritic cell vaccines in glioblastoma: An exploratory randomized phase II clinical trial. *Cancer Immunol. Immunother.* **2018**, *67*, 1777–1788. [[CrossRef](#)]
203. Zahradova, L.; Mollova, K.; Ocadlikova, D.; Kovarova, L.; Adam, Z.; Krejci, M.; Pour, L.; Krivanova, A.; Sandecka, V.; Hajek, R. Efficacy and safety of Id-protein-loaded dendritic cell vaccine in patients with multiple myeloma—phase II study results. *Neoplasma* **2012**, *59*, 440–449. [[CrossRef](#)]
204. Zemanova, M.; Cernovska, M.; Havel, L.; Bartek, T.; Lukesova, S.; Jakesova, J.; Vanasek, J.; Reiterer, P.; Kultun, J.; Andrasina, I.; et al. Autologous dendritic cell-based immunotherapy (DCVAC/LuCa) and carboplatin/paclitaxel in advanced non-small cell lung cancer: A randomized, open-label, phase I/II trial. *Cancer Treat. Res. Commun.* **2021**, *28*, 100427. [[CrossRef](#)] [[PubMed](#)]
205. Adams, A.M.; Carpenter, E.L.; Clifton, G.T.; Vreeland, T.J.; Chick, R.C.; O'Shea, A.E.; McCarthy, P.M.; Kemp Bohan, P.M.; Hickerson, A.T.; Valdera, F.A.; et al. Divergent clinical outcomes in a phase 2B trial of the TLPLDC vaccine in preventing melanoma recurrence and the impact of dendritic cell collection methodology: A randomized clinical trial. *Cancer Immunol. Immunother.* **2023**, *72*, 697–705. [[CrossRef](#)]
206. Ardon, H.; Van Gool, S.W.; Verschuere, T.; Maes, W.; Fieuws, S.; Sciot, R.; Wilms, G.; Demael, P.; Goffin, J.; Van Calenbergh, F.; et al. Integration of autologous dendritic cell-based immunotherapy in the standard of care treatment for patients with newly diagnosed glioblastoma: Results of the HGG-2006 phase I/II trial. *Cancer Immunol. Immunother.* **2012**, *61*, 2033–2044. [[CrossRef](#)] [[PubMed](#)]
207. Berntsen, A.; Trepiakas, R.; Wenandy, L.; Geertsens, P.F.; Thor Straten, P.; Andersen, M.H.; Pedersen, A.E.; Claesson, M.H.; Lorentzen, T.; Johansen, J.S.; et al. Therapeutic dendritic cell vaccination of patients with metastatic renal cell carcinoma: A clinical phase 1/2 trial. *J. Immunother.* **2008**, *31*, 771–780. [[CrossRef](#)] [[PubMed](#)]
208. Bulgarelli, J.; Piccinini, C.; Scarpi, E.; Gentili, G.; Renzi, L.; Carloni, S.; Limarzi, F.; Pancisi, E.; Granato, A.M.; Petrini, M.; et al. Adjuvant dendritic cell-based immunotherapy in melanoma: Insights into immune cell dynamics and clinical evidence from a phase II trial. *J. Transl. Med.* **2025**, *23*, 455. [[CrossRef](#)]
209. Everson, R.G.; Hugo, W.; Sun, L.; Antonios, J.; Lee, A.; Ding, L.; Bu, M.; Khattab, S.; Chavez, C.; Billingslea-Yoon, E.; et al. TLR agonists polarize interferon responses in conjunction with dendritic cell vaccination in malignant glioma: A randomized phase II Trial. *Nat. Commun.* **2024**, *15*, 4800. Erratum in *Nat. Commun.* **2024**, *15*, 3882. <https://doi.org/10.1038/s41467-024-48073-y..> [[CrossRef](#)]
210. Fucikova, J.; Podrazil, M.; Jarolim, L.; Bilkova, P.; Hensler, M.; Becht, E.; Gasova, Z.; Klouckova, J.; Kayserova, J.; Horvath, R.; et al. Phase I/II trial of dendritic cell-based active cellular immunotherapy with DCVAC/PCa in patients with rising PSA after primary prostatectomy or salvage radiotherapy for the treatment of prostate cancer. *Cancer Immunol. Immunother.* **2018**, *67*, 89–100. [[CrossRef](#)]
211. Garcia-Marquez, M.A.; Wennhold, K.; Draube, A.; von Bergwelt-Baildon, M. Results of a Phase II clinical trial with Id-protein-loaded dendritic cell vaccine in multiple myeloma: Encouraging or discouraging? *Immunotherapy* **2012**, *4*, 991–994. [[CrossRef](#)]
212. Chick, R.C.; Faries, M.B.; Hale, D.F.; Kemp Bohan, P.M.; Hickerson, A.T.; Vreeland, T.J.; Myers, J.W., 3rd; Cindass, J.L.; Brown, T.A., 2nd; Hyngstrom, J.; et al. Multi-institutional, prospective, randomized, double-blind, placebo-controlled phase IIb trial of the tumor lysate, particle-loaded, dendritic cell (TLPLDC) vaccine to prevent recurrence in high-risk melanoma patients: A subgroup analysis. *Cancer Med.* **2021**, *10*, 4302–4311. [[CrossRef](#)]
213. Coosemans, A.; Vanderstraeten, A.; Tuybaerts, S.; Verschuere, T.; Moerman, P.; Berneman, Z.N.; Vergote, I.; Amant, F.; SW, V.A.N.G. Wilms' Tumor Gene 1 (WT1)-loaded dendritic cell immunotherapy in patients with uterine tumors: A phase I/II clinical trial. *Anticancer. Res.* **2013**, *33*, 5495–5500.
214. Lee, J.M.; Lee, M.H.; Garon, E.; Goldman, J.W.; Salehi-Rad, R.; Baratelli, F.E.; Schae, D.; Wang, G.; Rosen, F.; Yanagawa, J.; et al. Phase I Trial of Intratumoral Injection of CCL21 Gene-Modified Dendritic Cells in Lung Cancer Elicits Tumor-Specific Immune Responses and CD8(+) T-cell Infiltration. *Clin. Cancer Res.* **2017**, *23*, 4556–4568. [[CrossRef](#)]

215. Chia, W.K.; Wang, W.W.; Teo, M.; Tai, W.M.; Lim, W.T.; Tan, E.H.; Leong, S.S.; Sun, L.; Chen, J.J.; Gottschalk, S.; et al. A phase II study evaluating the safety and efficacy of an adenovirus-DeltaLMP1-LMP2 transduced dendritic cell vaccine in patients with advanced metastatic nasopharyngeal carcinoma. *Ann. Oncol.* **2012**, *23*, 997–1005. [[CrossRef](#)] [[PubMed](#)]
216. Steele, J.C.; Rao, A.; Marsden, J.R.; Armstrong, C.J.; Berhane, S.; Billingham, L.J.; Graham, N.; Roberts, C.; Ryan, G.; Uppal, H.; et al. Phase I/II trial of a dendritic cell vaccine transfected with DNA encoding melan A and gp100 for patients with metastatic melanoma. *Gene Ther.* **2011**, *18*, 584–593. [[CrossRef](#)] [[PubMed](#)]
217. Saberian, C.; Amaria, R.N.; Najjar, A.M.; Radvanyi, L.G.; Haymaker, C.L.; Forget, M.A.; Bassett, R.L.; Faria, S.C.; Glitza, I.C.; Alvarez, E.; et al. Randomized phase II trial of lymphodepletion plus adoptive cell transfer of tumor-infiltrating lymphocytes, with or without dendritic cell vaccination, in patients with metastatic melanoma. *J. Immunother. Cancer* **2021**, *9*, e002449. [[CrossRef](#)] [[PubMed](#)]
218. Escudier, B.; Dorval, T.; Chaput, N.; Andre, F.; Caby, M.P.; Novault, S.; Flament, C.; Leboulleire, C.; Borg, C.; Amigorena, S.; et al. Vaccination of metastatic melanoma patients with autologous dendritic cell (DC) derived-exosomes: Results of the first phase I clinical trial. *J. Transl. Med.* **2005**, *3*, 10. [[CrossRef](#)]
219. Greene, J.M.; Schneble, E.J.; Jackson, D.O.; Hale, D.F.; Vreeland, T.J.; Flores, M.; Martin, J.; Herbert, G.S.; Hardin, M.O.; Yu, X.; et al. A phase I/IIa clinical trial in stage IV melanoma of an autologous tumor-dendritic cell fusion (dendritoma) vaccine with low dose interleukin-2. *Cancer Immunol. Immunother.* **2016**, *65*, 383–392. [[CrossRef](#)]
220. Poschke, I.; Lovgren, T.; Adamson, L.; Nystrom, M.; Andersson, E.; Hansson, J.; Tell, R.; Masucci, G.V.; Kiessling, R. A phase I clinical trial combining dendritic cell vaccination with adoptive T cell transfer in patients with stage IV melanoma. *Cancer Immunol. Immunother.* **2014**, *63*, 1061–1071. [[CrossRef](#)]
221. Chu, C.S.; Boyer, J.; Schullery, D.S.; Gimotty, P.A.; Gartner, V.; Bender, J.; Levine, B.L.; Coukos, G.; Rubin, S.C.; Morgan, M.A.; et al. Phase I/II randomized trial of dendritic cell vaccination with or without cyclophosphamide for consolidation therapy of advanced ovarian cancer in first or second remission. *Cancer Immunol. Immunother.* **2012**, *61*, 629–641. [[CrossRef](#)]
222. Dillman, R.O.; Cornforth, A.N.; Depriest, C.; McClay, E.F.; Amatruda, T.T.; de Leon, C.; Ellis, R.E.; Mayorga, C.; Carbonell, D.; Cubellis, J.M. Tumor stem cell antigens as consolidative active specific immunotherapy: A randomized phase II trial of dendritic cells versus tumor cells in patients with metastatic melanoma. *J. Immunother.* **2012**, *35*, 641–649. [[CrossRef](#)]
223. Dillman, R.O.; Cornforth, A.N.; Nistor, G.I.; McClay, E.F.; Amatruda, T.T.; Depriest, C. Randomized phase II trial of autologous dendritic cell vaccines versus autologous tumor cell vaccines in metastatic melanoma: 5-year follow up and additional analyses. *J. Immunother. Cancer* **2018**, *6*, 19. [[CrossRef](#)]
224. Faiena, I.; Comin-Anduix, B.; Berent-Maoz, B.; Bot, A.; Zomorodian, N.; Sachdeva, A.; Said, J.; Cheung-Lau, G.; Pang, J.; Macabali, M.; et al. A Phase I, Open-label, Dose-escalation, and Cohort Expansion Study to Evaluate the Safety and Immune Response to Autologous Dendritic Cells Transduced with AdGMCA9 (DC-AdGMCAIX) in Patients with Metastatic Renal Cell Carcinoma. *J. Immunother.* **2020**, *43*, 273–282. [[CrossRef](#)] [[PubMed](#)]
225. Dumoulin, D.W.; Cornelissen, R.; Bezemer, K.; Baart, S.J.; Aerts, J. Long-Term Follow-Up of Mesothelioma Patients Treated with Dendritic Cell Therapy in Three Phase I/II Trials. *Vaccines* **2021**, *9*, 525. [[CrossRef](#)] [[PubMed](#)]
226. Lau, S.P.; Klaase, L.; Vink, M.; Dumas, J.; Bezemer, K.; van Krimpen, A.; van der Breggen, R.; Wismans, L.V.; Doukas, M.; de Koning, W.; et al. Autologous dendritic cells pulsed with allogeneic tumour cell lysate induce tumour-reactive T-cell responses in patients with pancreatic cancer: A phase I study. *Eur. J. Cancer* **2022**, *169*, 20–31. [[CrossRef](#)]
227. Parney, I.F.; Anderson, S.K.; Gustafson, M.P.; Steinmetz, S.; Peterson, T.E.; Kroneman, T.N.; Raghunathan, A.; O'Neill, B.P.; Buckner, J.C.; Solseth, M.; et al. Phase I trial of adjuvant mature autologous dendritic cell/allogeneic tumor lysate vaccines in combination with temozolomide in newly diagnosed glioblastoma. *Neurooncol. Adv.* **2022**, *4*, vda089. [[CrossRef](#)]
228. Lemoine, F.M.; Cheraï, M.; Giverne, C.; Dimitri, D.; Rosenzweig, M.; Trebeden-Negre, H.; Chaput, N.; Barrou, B.; Thioun, N.; Gattegnio, B.; et al. Massive expansion of regulatory T-cells following interleukin 2 treatment during a phase I-II dendritic cell-based immunotherapy of metastatic renal cancer. *Int. J. Oncol.* **2009**, *35*, 569–581. [[CrossRef](#)]
229. Sonpavde, G.; McMannis, J.D.; Bai, Y.; Seethammagari, M.R.; Bull, J.M.C.; Hawkins, V.; Dancsak, T.K.; Lapteva, N.; Levitt, J.M.; Moseley, A.; et al. Phase I trial of antigen-targeted autologous dendritic cell-based vaccine with in vivo activation of inducible CD40 for advanced prostate cancer. *Cancer Immunol. Immunother.* **2017**, *66*, 1345–1357. [[CrossRef](#)]
230. Zhang, W.; Lu, X.; Cui, P.; Piao, C.; Xiao, M.; Liu, X.; Wang, Y.; Wu, X.; Liu, J.; Yang, L. Phase I/II clinical trial of a Wilms' tumor 1-targeted dendritic cell vaccination-based immunotherapy in patients with advanced cancer. *Cancer Immunol. Immunother.* **2019**, *68*, 121–130. [[CrossRef](#)]
231. Aerts, J.G.; Belderbos, R.; Baas, P.; Scherpereel, A.; Bezemer, K.; Enninga, I.; Meijer, R.; Willemsen, M.; Berardi, R.; Fennell, D.; et al. Dendritic cells loaded with allogeneic tumour cell lysate plus best supportive care versus best supportive care alone in patients with pleural mesothelioma as maintenance therapy after chemotherapy (DENIM): A multicentre, open-label, randomised, phase 2/3 study. *Lancet Oncol.* **2024**, *25*, 865–878. [[CrossRef](#)]

232. Bassani-Sternberg, M.; Digkila, A.; Huber, F.; Wagner, D.; Sempoux, C.; Stevenson, B.J.; Thierry, A.C.; Michaux, J.; Pak, H.; Racle, J.; et al. A Phase Ib Study of the Combination of Personalized Autologous Dendritic Cell Vaccine, Aspirin, and Standard of Care Adjuvant Chemotherapy Followed by Nivolumab for Resected Pancreatic Adenocarcinoma—A Proof of Antigen Discovery Feasibility in Three Patients. *Front. Immunol.* **2019**, *10*, 1832. [[CrossRef](#)]
233. Franssen, L.E.; Roeven, M.W.H.; Hobo, W.; Doorn, R.; Oostvogels, R.; Falkenburg, J.H.F.; van de Donk, N.W.; Kester, M.G.D.; Fredrix, H.; Westinga, K.; et al. A phase I/II minor histocompatibility antigen-loaded dendritic cell vaccination trial to safely improve the efficacy of donor lymphocyte infusions in myeloma. *Bone Marrow Transplant.* **2017**, *52*, 1378–1383. [[CrossRef](#)]
234. Gowans, E.J.; Roberts, S.; Jones, K.; Dinatale, I.; Latour, P.A.; Chua, B.; Eriksson, E.M.; Chin, R.; Li, S.; Wall, D.M.; et al. A phase I clinical trial of dendritic cell immunotherapy in HCV-infected individuals. *J. Hepatol.* **2010**, *53*, 599–607. [[CrossRef](#)]
235. Curti, A.; Tosi, P.; Comoli, P.; Terragna, C.; Ferri, E.; Cellini, C.; Massaia, M.; D’Addio, A.; Giudice, V.; Di Bello, C.; et al. Phase I/II clinical trial of sequential subcutaneous and intravenous delivery of dendritic cell vaccination for refractory multiple myeloma using patient-specific tumour idiotype protein or idiotype (VDJ)-derived class I-restricted peptides. *Br. J. Haematol.* **2007**, *139*, 415–424. [[CrossRef](#)]
236. Bol, K.F.; Schreibelt, G.; Bloemendal, M.; van Willigen, W.W.; Hins-de Bree, S.; de Goede, A.L.; de Boer, A.J.; Bos, K.J.H.; Duiveman-de Boer, T.; Olde Nordkamp, M.A.M.; et al. Adjuvant dendritic cell therapy in stage IIIB/C melanoma: The MIND-DC randomized phase III trial. *Nat. Commun.* **2024**, *15*, 1632. [[CrossRef](#)]
237. Tryggestad, A.M.A.; Axcrona, K.; Axcrona, U.; Bigalke, I.; Brennhovd, B.; Inderberg, E.M.; Honnashagen, T.K.; Skoge, L.J.; Solum, G.; Saeboe-Larssen, S.; et al. Long-term first-in-man Phase I/II study of an adjuvant dendritic cell vaccine in patients with high-risk prostate cancer after radical prostatectomy. *Prostate* **2022**, *82*, 245–253. [[CrossRef](#)]

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