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Review Article

Efficacy of Adoptive Cell Therapy with Natural Killer Cells in Cases of Solid Tumors

Diana Esquivel[1], Laura de Jesús[2], Evangelina Galindo[2], Christoper Martinez[2], Brandon Rodríguez[2], Rangnath Mishra[1,3], Anand Srivastava[1,3]*

[1]Global Institute of Stem Cell Therapy and Research, México. Calle 289 Alamo, Suite 5, Vicente Guerrero, 21970 Los Algodones, Baja California.

[2]Universidad del Valle de México, Campus Mexicali. Calle Novena 294, Plutarco Elías Calles, C.P. 21396, Mexicali Baja California.

[3]GIOSTAR USA, 4660 La Jolla Village Drive, 1st Floor, San Diego, California 92122, U.S.A.

***Corresponding author:** Srivastava A, Global Institute of Stem Cell Therapy and Research, México. Calle 289 Alamo, Suite 5, Vicente Guerrero, 21970 Los Algodones, Baja California.

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Abstract

Background: Cancer remains one of the leading causes of mortality worldwide and poses major therapeutic challenges due to tumor heterogeneity, an immunosuppressive tumor microenvironment, and immune evasion. Adoptive Natural Killer (NK) cell therapy has emerged as a promising immunotherapeutic strategy because of its ability to recognize and eliminate tumor cells independently of major histocompatibility complex (MHC) restriction while maintaining a favorable safety profile. **Methods:** This systematic review was conducted according to PRISMA guidelines. PubMed and Google Scholar were searched for clinical studies published within the last 20 years evaluating adoptive NK cell therapy for lung, breast, and colorectal cancer. Study characteristics, NK cell processing and administration protocols, and clinical outcomes were analyzed. Of 21,554 records identified, 20 studies met the inclusion criteria. **Results:** Most studies focused on non-small cell lung cancer and predominantly used allogeneic peripheral blood-derived NK cells. Peripheral blood was the main cell source (75%), while allogeneic NK cells accounted for 60% of therapeutic approaches. Fourteen studies (70%) reported significant improvements in at least one clinical outcome, including overall survival, progression-free survival, objective tumor response, tumor biomarkers, or quality of life. NK cell therapy demonstrated a favorable safety profile, with mainly mild to moderate adverse events. However, substantial heterogeneity was observed in cell sources, expansion protocols, infused cell doses, and treatment schedules. **Conclusions:** Adoptive NK cell therapy shows considerable potential as a complementary treatment for solid tumors. Nevertheless, larger multicenter clinical trials using standardized manufacturing protocols and harmonized outcome measures are needed to establish its clinical efficacy.

Keywords: Cancer; Natural Killer Cells; NK Therapy; Solid Tumors; Systematic Review.

Introduction

Recent scientific and technological advances have emerged with new paradigms in the understanding of cancer pathobiology. Today, we recognize that cancer is not simply a disease, but a complex systemic manifestation of the interactions of normal cells with their microenvironment, leading to the formation of cancerous cells [1]. Development of this multifaceted disease involves different processes in addition to mutations at the genetic level. The interaction of epigenetic events, metabolic dysregulation, and evasion from the immune surveillance, among others, eventually leads to the development of this condition, a complex process known as carcinogenesis [2]. Globally, 20 million new cases of cancer were estimated in 2022, with 9.7 million deaths in that year. According to WHO on average 1 in every 5 people develops one or another type of cancer in their lifetime [3]. Historically, surgical procedures as well as chemotherapy have been the first treatment options for almost every type of cancer. However, surgery may not be a viable option due to the complexity caused by the anatomical location of a solid tumor, while the cost incurred due to the compromised quality-of-life of patients receiving chemotherapy is often very high [4]. Therefore, the demands for development of new therapeutic approaches focused on enhancing the immune system's ability to recognize and eliminate cancer cells have surged in recent years. Mainly, the use of adoptive cell therapies, with the aim of potentiating the patient's immune activity, has shown promising results in cases of solid tumors. Within the different lines of research, the use of natural killer (NK) cells has stood out for their high cytotoxic capacity in addition to their ability to recognize cancer cells [5]. Despite the fact that there is a growing understanding of the mechanism of action of NK cells [6], there are not many studies that systematically analyze the efficacy of this adoptive cell therapy using NK cells in such cases. Therefore, the objective of this study is to present a timely literature review on cancer and different therapies used in its treatment, as well as a systematic analysis of the efficacy of NK cell therapy in solid tumor cases.

Literary Review

Carcinogenesis Process

Carcinogenesis is a sum of a number of processes by which a normal cell acquires changes, including genetic alterations that enable uncontrolled growth and the ability to evade surveillance mechanisms, thereby giving rise to a neoplasm [7]. This mechanism can be driven by inherited genetic mutations or by the progressively accumulated genetic mutations, which eventually convert proto-oncogenes into active oncogenes, as well as to inactivate tumor suppressor genes (such as RB1) and DNA repair genes (such as BRCA1/2). As a consequence, a cell acquires the ability to proliferate in an uncontrolled manner, which leads to the expansion of cell clones with selective advantages [8]. This transformation is not a single event, but a cumulative outcome of a series of genetic and epigenetic alterations that confer abnormal biological capacities to a normal cell, known as the "Hallmarks of Cancer" or Cancer Markers [9]. These capabilities include constant proliferation in suboptimal environments, evasion from tumor suppression and elimination mechanisms, and resistance to programmed cell death, leading to the development of metastasis. Interestingly, their temporal order of appearance has recently been elucidated at the genomic level, showing that genomic instability is usually the first event, while immune evasion tends to be the last [9, 10]. Brown and colleagues [11] correctly suggested not to view cancer as a simple uncontrolled growth only, but as a miniature ecosystem "subject to evolution by natural selection".

Cancer has two main variants depending on its physical nature: solid tumorous or non-solid cancerous. Non-solid cancers arise in bone marrow and lymphoid tissues, and the tumor cells keep circulating in the blood. Although they do not form any distinguishable cell masses, they share the basic mechanisms of cell transformation and evolution typical of this condition [12]. On the other hand, solid tumors develop in distinguishable specific tissue masses, generating organized but undesired structures. Three key elements needed for its development are: accumulation of oncogenic changes, uncontrolled cell division, and an extracellular environment that supports the survival of abnormal cells. These altered cells acquire proliferative autonomy, escaping the immune-vigilance controls. The current literature indicates that they undergo a set of crucial biological change as they cease to act as an integral part of the organism and operate as independent entities [12]. This process involves a gradual loss of the mechanisms that normally regulate cell division and specialization. The transformed cells evade programmed death signals, modify their metabolism, and become independent of systemic factors that also contribute to restricting their growth [9].

Another important factor that contributes to the worsening of the patient's condition is the tumors' own microenvironment, as these populations of cancer cells are not identical or homogeneous. In addition to already present heterogeneity, other hereditary variations constantly arise. Initially, the immune system eliminates many of these cells, but these acquired mutations lead to exhaustion of surveillance machinery [13]. In this microenvironment, tumors can also reprogram stromal cells as fibroblasts, recruit protumor cell populations, and induce processes that collectively benefit the neoplastic population, such as angiogenesis and the synthesis of various components of the extracellular matrix. This continuously evolving process leads to tumor adaptation, including metastasis

as well as resistance to therapies [11].

Finally, both solid and non-solid tumors advance according to evolutionary principles operating at the cellular level. Cancer cell populations show heritable genetic and epigenetic diversities, which enable their better survival than normal cells. In suboptimal conditions, such as lesser availability of nutrients and space, lack of oxygen, higher acidity, and absence of the host's immune responses within the tumor microenvironment promote the growth of subpopulations with adaptive advantages [12]. This process further intensifies in clinical manifestations such as metastasis and generalized resistance to therapies. Understanding all cancers through this unified framework that combines cell transformation and evolution by selection can provide a foundation for creating novel therapies. In particular, it points to the need for approaches that recognize the dynamic and adaptable nature of cancer cells, as well as the importance of targeting multiple survival and proliferation pathways at the same time, beyond conventional anatomical classification [9, 12, 14].

Conventional Cancer Treatments

The burden of solid cancers has increased greatly in recent years all around the globe and today represents one of the main public health concerns According to global data from GLOBOCAN, the most commonly diagnosed cancers are lung cancer (20%), breast cancer (19%), colorectal cancer (16%), prostate cancer (12%), and stomach cancer (8%). All other types of cancer together account for the remaining 25% [15, 16]. Although these percentages are adjusted for clarity purposes, they maintain the overall proportion observed in actual epidemiology, where lung cancer continues to be the leading cause of cancer death in the world [16]. The WHO notes that the total number of cases will continue to grow due to an increasing aging population and along with higher exposure to risk factors such as smoking and obesity; which are further potentiated by the limited access to medical services. This scenario becomes a global challenge, and dealing with it requires improvements in preventative measures, such as regular health check-ups to facilitate timely diagnosis and easy access to treatment [3].

Because of the global social and economic burden of these types of conditions, many resources have been allocated to investigate new, more effective ways of dealing with cancer. Clinical approaches include multiple modalities, mainly surgical, chemical, and biochemical treatments. Their efficacy depends, to a large extent, on the immunosuppressive tumor microenvironment (TME), pH, cell heterogeneity, and the patient's immunological and clinical status. However, in cases of solid tumors, several factors significantly limit the penetration of drugs and the activation of the immune system, compromising the achievement of complete eradication [17].

Surgery remains one of the most common options for trying to eliminate many solid tumors when they are diagnosed in early stages. After surgery, adjuvant treatments (such as chemotherapy or radiation therapy) are often given to eliminate or at least decrease the risk of the cancer coming back. In other cases, when the tumor is large or difficult to remove surgically, treatments such as chemotherapy are usually prescribed to reduce the size of the tumor before surgery. However, in advanced or metastatic stages, the most commonly used conventional treatments are chemotherapy and radiotherapy [18, 19].

Many chemotherapeutic agents are in use for addressing different types of cancers. These mainly act through cytotoxic mechanisms, causing DNA damage, inhibiting replication, and inducing apoptosis in preferably highly proliferating cells. However, chemotherapy often comes up with several undesired side effects and can lead to lymphopenia and systemic immunosuppression. These limitations underscore the need to optimize the dosage and combination of other therapies to maximize their efficacy in advanced treatment regimens [20, 21].

On the other hand, physical therapies use different energy sources to induce structural damage and local cell death. Physical treatments include radiotherapy (RT), which uses ionizing radiation to induce DNA damage and trigger apoptosis [17]. Another modality is photodynamic therapy (PDT) that combines light with a photosensitizer to induce necrosis. Finally, photothermal phototherapy (PTT) using a laser and thermal conversion, which produces thermal ablation of the tumor. A relevant aspect of these technologies is that, in addition to direct damage to the tumor, they can induce immunogenic cell death (ICD), releasing danger signals (DAMPs) that reactivate the immune system, giving rise to therapies combined with immune checkpoint inhibitors (ICIs) or cellular immunotherapy [22]. However, its main limitation arises from the immunosuppressive tumor microenvironment, which can block this response, recruit inhibitory cells, and express molecules such as PD-L1 that compromise the cytotoxic action of lymphocytes [17, 23].

Over the past decade, biologic therapies have revolutionized cancer treatment by using components of the immune system, such as antibodies, cytokines, oncolytic viruses, and, more recently, genetically modified immune cells. Among these, T cells with chimeric antigen receptors (CAR-T) stand out, demonstrating long-term remissions in hematological cancers [24]. However, its efficacy in solid tumors is limited due to its inability to infiltrate the dense tumor masses and poor performance in immunosuppressive microenvironments. Faced with these challenges, natural killer (NK) cell therapy emerges as an alternative with great potential. Unlike T cells, NK cells have an innate ability to recognize and eliminate tumor cells without the need for antigen presentation

via the major histocompatibility complex (MHC). NK cells also produce immunostimulatory cytokines such as interferon gamma (IFN-γ), which lowers the risk of graft-versus-host disease (GVHD) compared to T cells. These advantages position NK-cell-based therapies as promising options, especially for solid tumors where CAR-T cells have faced greater limitations [25].

Finally, it is important to note that the choice of treatment varies greatly depending on the type of cancer, stage at time of diagnosis, present comorbidities, and health system resources. The incorporation of targeted therapies and immunotherapies has changed the landscape for certain tumors [18, 26].

Adoptive Cell Therapy with Natural Killers

There is a growing interest in adoptive cell therapies using Natural Killer cells due to several biological advantages they present in contrast to other types of immunotherapies. One of the most important aspects is that they do not require the major histocompatibility complex (MHC), which allows their use in autologous, allogeneic, or genetically modified platforms, allowing their standardized and cost-effective production.

The insertion of chimeric antigen receptors (CAR) into NK cells allows their cytotoxic activity to be specifically directed against tumor cells expressing specific antigens. This strategy combines both the natural ability of NK cells to recognize stressed or low-expression MHC-I cells and the specificity conferred by CAR [27]. Despite these advantages, CAR-NK cells are not without limitations. Their effectiveness is usually short as they have a low capacity to infiltrate into the solid tumors, and they could be inhibited by the tumor microenvironment, especially by factors such as the cytokine TGF-β, hypoxia, or the accumulation of adenosine. These barriers represent a significant challenge for their application in solid tumors, where even CAR-T therapy has yielded limited clinical success [28].

Nevertheless, NK therapies do not have serious adverse effects, such as graft-versus-host syndrome (GVHD), cytokine release syndrome (CRS), or neurotoxicity associated with modified lymphocyte therapies. This has positioned NK as a potentially safer alternative that is easier to implement clinically [29]. Finally, it is important to recall that CAR-NK cell immunotherapy represents a complementary treatment against cancer, which could be used alongside with other treatments, such as chemotherapies and radiotherapies.

Methodology

Article Search Using PRISMA Methodology

A systematic literature review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, with the aim of compiling and analyzing current evidence regarding the efficacy of adoptive Natural Killer (NK) cell therapy in solid tumors, specifically lung, breast, and colon cancer, due to their high global incidence and economic burden.

The bibliographic search was performed using the PubMed and Google Scholar databases. The search strategy included the following keywords: “NK immunotherapy”, “adoptive NK cell”, “allogeneic NK cell”, and “autologous NK cell”. These terms were subsequently combined with “lung cancer”, “breast cancer”, or “colon cancer” to focus the search on the selected types of cancer.

Inclusion Criteria

Original articles, clinical studies, and case reports evaluating the efficacy of NK cell-based immunotherapy in solid tumors, specifically lung, breast, and colon cancer, were included. Studies in which NK cells were administered either as monotherapy or in combination with chemotherapy and/or radiotherapy were considered eligible. Both non-modified and genetically modified NK cells were included. Ultimately, studies involving patients with metastatic disease were not excluded.

Exclusion Criteria

Studies published more than 20 years prior to the search date and those published in languages other than English were excluded. Studies not specifically focused on the selected cancer types were also excluded. In addition, review articles, meta-analyses, editorials, comments, in vitro studies using tumor biopsies, and animal model studies were excluded. Finally, studies employing immunotherapeutic strategies other than NK cells (such as CAR-T cells or dendritic cell therapies) were excluded in order to better isolate the therapeutic effect attributable to NK cell therapy.

The quantitative analysis focused on evaluating the clinical efficacy of NK cell therapy. For this purpose, general study characteristics, cohort size, and clinical phase were systematically extracted. Similarly, laboratory processing methods, including NK cell culture and activation protocols, as well as the dose and number of infusions administered, were analyzed. Finally, the review examined the scales and clinical endpoints used to evaluate therapeutic efficacy in patients.

Data Extraction

In Google Scholar, the search strategy yielded a considerably high number of results (exceeding one million records depending on the keyword combination). To ensure the feasibility and systematic nature of the review, approximately 1,500 records were screened for each keyword combination and cancer type (12 combinations in total), resulting in approximately 18,000 records considered during the initial selection process.

Together with records identified through PubMed (n = 3,554), a total of 21,554 records were initially identified. After applying

filters related to publication period (last 20 years), English language, study type (excluding reviews and meta-analyses), and human studies, 18,997 records were excluded, resulting in 2,557 records eligible for screening.

During the screening phase, 2,534 records were excluded for not meeting the inclusion criteria, including non-eligible study designs or irrelevant therapeutic approaches (such as CAR-T or other immunotherapies). Consequently, 23 full-text articles were assessed for eligibility.

Finally, 3 studies were excluded after full-text evaluation due to insufficient methodological information or lack of relevance to the selected pathologies. Therefore, a total of 20 studies were included in the final systematic review (Figure1).

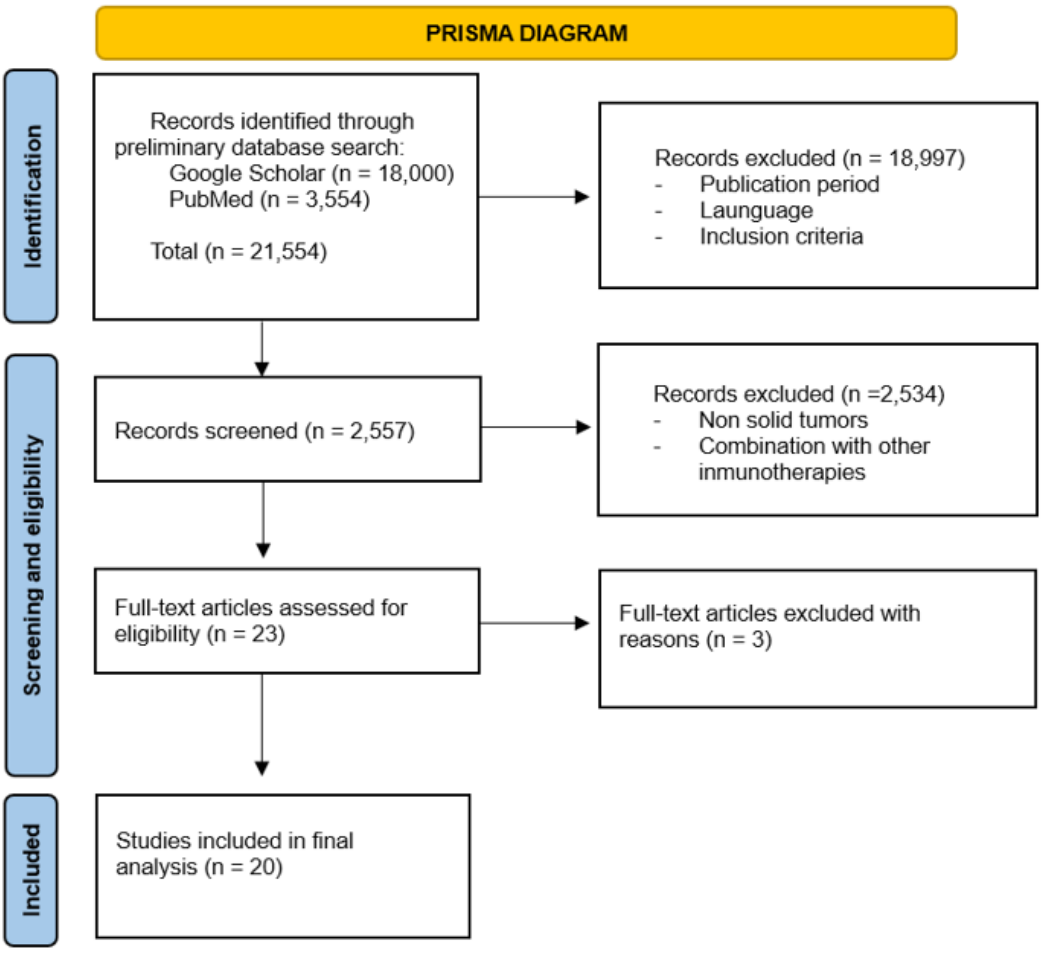


Figure 1: PRISMA flow diagram of literature search and included publications.

Results

General criterion of the included studies

Among the 20 studies analyzed, the most frequent cancer type was non-small cell lung cancer (NSCLC), representing 70% (n = 14) of the included studies, followed by breast cancer with 15% (n = 3), colon carcinoma with 5% (n = 1), and colon adenocarcinoma with 10% (n = 2). Regarding the type of immunotherapy used, allogeneic NK cell therapy predominated, accounting for 60% (n = 12) of the studies, whereas autologous NK therapy represented 35% (n = 7). In addition, one comparative study (5%, n = 1) evaluated both therapeutic approaches.

Most studies included relatively small patient populations, while only two studies (10%) enrolled more than 100 participants. Furthermore, metastatic disease was frequently reported among the study populations, being present in 45% (n = 9) of the studies, whereas 20% (n = 4) included non-metastatic patients and 35% (n = 7) did not report this information (NR).

As for simultaneously therapies, chemotherapy (CHT) was the most commonly used, reported in 55% (n = 11) of the studies; followed by radiotherapy (RT) in 30% (n = 6); surgery (SG) in 15% (n = 3), and adjuvant therapy (AT) in 30% (n = 6). In contrast, some studies did not report this information (NR), in 20% (n = 4), or the information was not classified (NC) in 5% (n = 1).

In terms of geographical distribution, China accounted for the highest proportion of publications, representing 45% (n = 9) of the included studies, while the remaining studies were distributed across different countries. Concerning age range, 65% (n = 13) of the studies included patients between 30 and 80 years old, whereas the remaining studies either included adults older than 18 years or did not specify patient age.

Regarding the phase of investigation, Phase I and combined Phase I/II studies predominated, accounting for 55% (n = 11) of the included studies. The remaining studies either did not report this information or corresponded to pilot studies and case reports, representing 45% (n = 9) (Table 1).

Laboratory processing and NK cell infusion in patients

Among the reviewed studies, peripheral blood was the predominant cellular source for NK cell isolation, accounting for 75% of the studies, whereas 10% used umbilical cord blood and another 10% employed leukapheresis-derived products. Notably, one study did not specify the cellular source.

Regarding the type of therapy, activated NK cells were the most commonly used approach, representing approximately 60% of the studies, followed by highly activated NK cells with 20%. More specialized therapies, including NKTm, NK sIL15_TRACK, and AIET NK, accounted for 5%, 5%, and 10% of the studies, respectively.

Concerning expansion and activation protocols, IL-2 was the most frequently used cytokine, being reported in approximately 40% (n = 8) of the reviewed studies, either alone or in combination with IL-12, IL-15, IL-18, or OK432. Commercial protocols such as HANK and BINKIT were also recurrently employed, representing 20% and 10% of the studies, respectively. Additionally, specialized culture media including AIM-V, α-MEM, and Aly505 were used in 10%, 5%, and 10% of the studies, respectively. Overall, these findings indicate that *ex vivo* cytokine-based expansion, particularly IL-2-mediated activation, remains the predominant strategy for NK cell proliferation and activation before clinical administration.

Regarding therapeutic administration, substantial heterogeneity was observed both in the number of infusions and in the quantity of NK cells administered. Most studies performed between 1 and 6 infusions (55%, n = 11)), although some protocols reached up to 12 repeated administrations. Approximately 40% of the studies administered doses equal to or greater than 10^9 NK cells per infusion, whereas others used lower concentrations ranging from 10^6 to 10^8 cells/kg.

HANK-based protocols consistently employed the highest cellular doses, reaching between 8–10 × 10^9 NK cells per infusion. In contrast, protocols using IL-2, IL-15, and OK432 generally administered intermediate cell quantities, ranging from 2–5 × 10^9 cells. Importantly, 30% (n = 6) of the studies did not fully report either the number of infused cells or the total number of treatment cycles, highlighting the methodological heterogeneity among the included studies (Figure 2, Table 2).

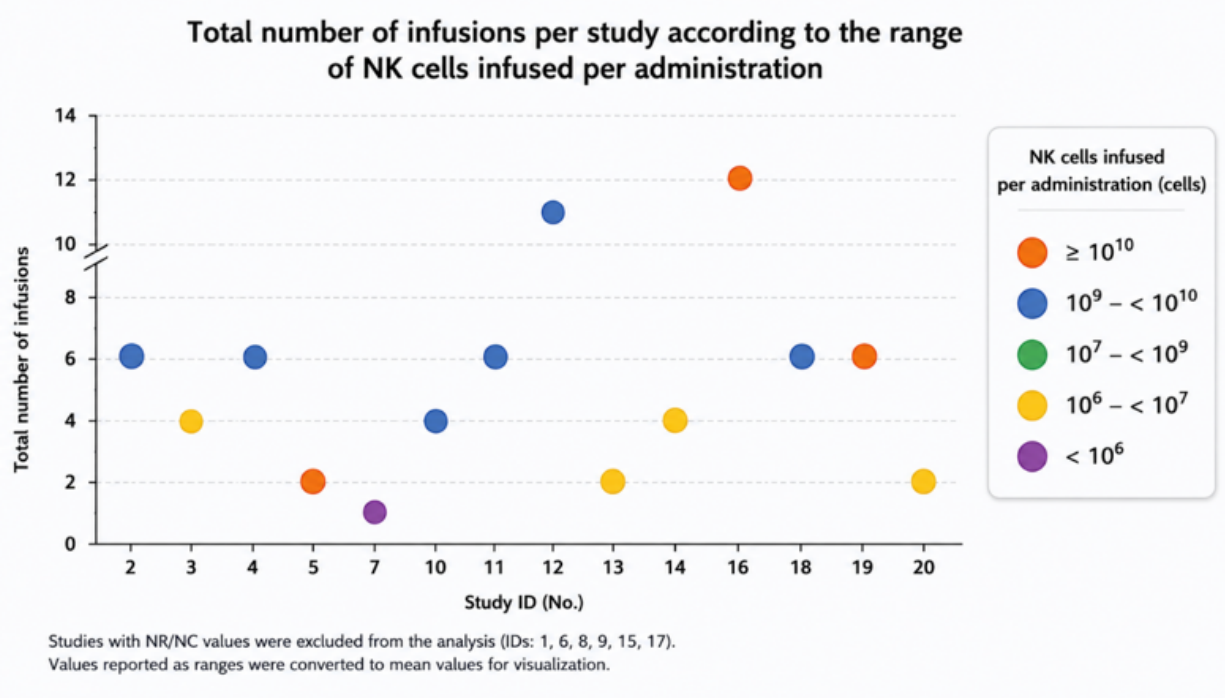


Figure 2: Distribution of the total number of NK cell infusions administered across the analyzed studies according to the range of NK cells infused per administration. Each point represents an individual study, while colors indicate the approximate range of NK cells administered per infusion. Studies with non-reported (NR) or non-classified (NC) data were excluded from the analysis. Cell ranges reported as intervals were converted to mean values for visualization purposes.

Efficacy of NK cell therapy in solid tumor cases

Based on the analysis of the included studies (Table 3), the most frequently used criteria to evaluate NK cell therapy efficacy were RECIST, overall survival (OS), and progression-free survival (PFS). RECIST was the most commonly employed assessment method, being reported in 50% (n = 10) of the studies, followed by OS and PFS, both used in 40% (n = 8) of the studies. These findings indicate that most studies evaluated tumor response and patient clinical evolution using standardized and widely accepted clinical endpoints.

Overall, the reviewed studies demonstrated favorable outcomes regarding the efficacy of NK cell therapy. A total of 70% (n = 14) of the studies reported statistically significant differences either when comparing treated groups with control groups or when evaluating pre- and post-treatment outcomes. Reported improvements included increased overall survival and progression-free survival, reduction in tumor size, decreased tumor marker levels, improved quality of life, increased response rates, and better disease control. Collectively, these findings suggest a consistent and positive therapeutic effect of NK cell therapy across different solid tumor types.

Regarding safety, 40% (n = 8) of the studies reported treatment-related adverse events, which were generally mild to moderate in severity and included fever, fatigue, pain, cough, nausea, and metabolic alterations. In contrast, 30% (n = 6) of the studies reported no adverse events, while another 30% (n = 6) did not provide information regarding safety outcomes. These findings suggest a generally favorable safety profile, although variability in adverse event reporting remains evident among studies.

Notably, only one study (5%) directly compared allogeneic and autologous NK cell therapies. In this comparative study, the allogeneic NK group demonstrated significantly improved outcomes, including greater reduction of circulating tumor cells, decreased tumor marker levels, better RECIST-based responses, and improved quality of life compared with the autologous group.

Discussion

General criterion of the included studies

The distribution of the included studies reflects the growing interest in evaluating the efficacy of NK cell-based therapies in solid tumors, particularly non-small cell lung cancer (NSCLC).

Most of the available evidence focused on NSCLC, likely due to its high global incidence and mortality, which continue to drive the development of novel therapeutic strategies [16]. Likewise, a substantial proportion of the studies were conducted in China, probably reflecting the remarkable expansion of cellular immunotherapy research in this region over the past decade. Although this has significantly contributed to the generation of clinical evidence, it also highlights the need to expand clinical trials to other geographical regions in order to determine whether these findings can be consistently reproduced across populations with different genetic, demographic, and clinical characteristics.

Another notable finding was the predominance of allogeneic NK cell therapies, suggesting a growing preference for strategies based on healthy donor-derived cells, which generally exhibit greater cytotoxic functionality and facilitate standardized large-scale manufacturing for clinical applications [50, 51]. Furthermore, NK cell therapy was rarely administered as a standalone treatment. Instead, it was commonly combined with other conventional therapies like chemotherapy, radiotherapy, surgery, or antibody-based therapies (Table 1), reflecting current efforts to enhance antitumor responses through multimodal therapeutic approaches [52, 53]. However, these combination strategies also complicate the interpretation of clinical outcomes, making it difficult to determine the extent to which the observed therapeutic benefit can be exclusively attributed to NK cell therapy.

#	Cancer type	Source type	No. of patients	Metastasis	Additional therapies	Reference
1	NSCLC	Allogenic	108	NR	SG, CHT, RT	[30]
2		Autologous	1	NR	AT, CHT, RT	[31]
3		Allogenic	16	YES	CHT	[32]
4		Allogenic	19	NO	AT, CHT	[33]
5		Allogenic	31	NO	NR	[34]
6		Allogenic	60	YES	CHT	[35]
7		Allogenic	6	NR	CHT, AT	[36]
8		Allogenic	109	NT	AT	[37]
9		Autologous	20	YES	CHT	[38]
10		Autologous	16	YES	CHT, RT	[39]
11		Autologous	18	YES	CHT, AT	[40]
12		Autologous	20	YES	CHT, AT	[41]
13	SCLC	Allogenic	1	YES	AT, RT	[42]
14	Pulmonary carcinoma	Autologous	1	NO	CHT, RT, AT	[43]
15	Breast cancer	Autologous	1	NO	CHT, RT	[44]
16		Autologous/Allogeneic	36	NR	NC	[45]
17		Allogenic	60	YES	SG, CHT	[46]
18	Colon carcinoma	Autologous	27	NR	CHT	[47]
19	Colon adenocarcinoma	Autologous	1	YES	SG, CHT	[48]
20		Autologous	1	YES	SG, CHT	[49]

NSCLS: Non-small-cell lung cancer; SCLC: Small-cell lung cancer; NR: Not reported; PS: Pilot study; CS: Case report; OPCS: Open-label Prospective Cohort Study; SG: Surgery; CHT: Chemotherapy; RT: Radiotherapy; AT: Antibody therapy; NR: Not reported; NT: Not clear.

Table 1: General characteristics of the studies included.

Additionally, most studies included relatively small patient cohorts, whereas only a limited number enrolled more than 100 participants, reducing the statistical robustness and generalizability of the available evidence. Overall, these findings indicate that although NK cell therapy represents a promising therapeutic strategy for solid tumors, larger multicenter clinical trials with standardized methodologies will be necessary to establish its true clinical efficacy.

Laboratory processing and NK cell infusion in patients

One of the most consistent findings of this review was the predominant use of peripheral blood as the primary source of NK cells. This preference is likely explained by the relative ease of sample collection, the possibility of repeated leukapheresis procedures when required, and the extensive clinical experience associated with peripheral blood-derived cellular products. Although alternative sources such as umbilical cord blood offer potential advantages, including greater proliferative capacity and the availability of more immature NK cell populations, their clinical implementation remains more limited due to the specialized infrastructure required for collection, processing, and storage [28].

Similarly, IL-2 was the cytokine most frequently incorporated into *ex vivo* expansion protocols, either alone or combined with IL-12, IL-15, IL-18, or other immunomodulatory agents. This observation is consistent with the well-established role of IL-2 in promoting NK cell proliferation, survival, and cytotoxic activity through the upregulation of perforin, granzymes, and IFN-γ production [54]. Commercial expansion platforms, particularly the HANK protocol, were also frequently employed, likely because they provide standardized manufacturing procedures, reduce technical variability, and facilitate compliance with quality standards required for clinical-grade cell production.

Despite these common trends, one of the major findings of this review was the considerable heterogeneity observed across treatment protocols. Both the number of NK cell infusions and the number of cells administered varied substantially among studies, with no clearly established therapeutic regimen emerging as the standard of care (Figure 2). This variability likely reflects the current developmental stage of NK cell therapy, in which different research groups continue to optimize dosing schedules, infusion frequency, and expansion protocols to maximize antitumor efficacy while maintaining an acceptable safety profile.

The lack of methodological standardization also limits direct comparisons between studies. Variations in cell source, expansion protocols, cytokine combinations, infused cell dose, and treatment schedule may all influence the functional activity of NK cells and ultimately affect clinical outcomes. Furthermore, approximately one-third of the included studies failed to report essential manufacturing information, including the number of infused cells or details of the expansion process, reducing reproducibility and hindering the identification of variables associated with improved therapeutic responses (Table 2). Collectively, these findings emphasize the importance of establishing standardized manufacturing protocols and more comprehensive methodological reporting in future clinical trials.

#	NK therapy	Source	Laboratory protocol
1	NKTm	Peripheral blood	Cell culture and expansion with OKM 25,100,200 medium
2	Activated NK	Peripheral blood	Cell culture and expansion with AIM-V + IL-2, IL-12, IL-18
3	Activated NK	Peripheral blood	Cell culture and expansion with α-MEM + IL-15
4	Activated NK	Peripheral blood	Cell cultured with IL-2, L-glutamine, anti CD3, anti-CD16, anti-CD56
5	Highly activated NK	Peripheral blood	HANK protocol
6	Highly activated NK	Peripheral blood	HANK protocol
7	NK sIL15_TRACK	Umbilical cord blood	Cell culture and expansion + anti-PD-L1
8	Highly activated NK	Peripheral blood	HANK protocol
9	Activated NK	Peripheral blood	Cell culture with Aly505 medium + IL-2, IL-15, OK432
10	Activated NK	Peripheral blood	Cell culture and expansion with TKD + IL-2
11	Activated NK	Peripheral blood	Cell culture and expansion
12	Activated NK	Leukapheres of peripheral blood	Cell culture with Aly505 medium + IL-2, IL-15, OK432
13	Activated NK	Umbilical cord blood	Cell culture and expansion + anti-PD-L2

14	Activated NK	Leukapheres of peripheral blood	Cell culture with TKD + IL-2
15	AIET NK	Peripheral blood	BINKIT expansion kit
16	Highly activated NK	Peripheral blood	HANK protocol
17	AIET NK	Peripheral blood	BINKIT expansion kit
18	Activated NK	Peripheral blood	Cell culture and expansion with AIM-V + IL-2, OK432
19	Activated NK	Peripheral blood	Cell culture with TKD + IL2
20	Activated NK	Peripheral blood	Cell culture and expansion
HANK: Human high activity NK cell in vitro preparation kit; AIET: Cell based autologous immune enhancement therapy; NT: Not clear.			

Table 2: Laboratory processing and NK cell infusion in patients.

Efficacy on NK cell therapy in solid tumors

Overall, the studies included in this review demonstrated a favorable trend regarding the clinical efficacy of NK cell-based therapies in solid tumors. Most investigations reported improvements in clinically relevant outcomes, including overall survival (OS), progression-free survival (PFS), objective tumor response, and patient quality of life. These findings are consistent with recent reviews highlighting the therapeutic potential of NK cells, largely attributed to their intrinsic ability to recognize and eliminate malignant cells independently of major histocompatibility complex (MHC)-restricted antigen recognition [56, 57]. Collectively, the available evidence supports the incorporation of NK cell therapy as a promising component within the evolving landscape of cancer immunotherapy.

Therapeutic efficacy was primarily evaluated using RECIST criteria, followed by survival outcomes such as OS and PFS. The widespread use of RECIST is likely explained by its acceptance as the standard imaging-based method for assessing objective tumor responses (Table 3). Nevertheless, the unique characteristics of immunotherapies present important challenges for the exclusive interpretation of RECIST, since phenomena such as pseudoprogression and delayed responses may not accurately reflect the true clinical benefit achieved by immune-based treatments [57, 58]. Consequently, incorporating immune-specific response criteria such as iRECIST, together with survival endpoints, immunological biomarkers, and patient-reported quality-of-life outcomes, may provide a more comprehensive evaluation of NK cell therapy.

#	Secondary adverse events	Deaths reported	Scale used	Outcome in treated group
1	Fever or skin erythema	Yes, in all groups	OS	2-year survival*
2	No	No	Size of tumor	Reduction by 50% approx.
			QOL	Improved
3	No	Yes, in all groups	RECIST	13.3% PR; 40% SD; 46.6% PD
			OS	Tendency to improve after 4 doses
			PFS	Tendency to improve after 4 doses
4	No	No	PFS	3 months
			RECIST	10.5% PR; 63% SD; 26% PD
			ODCR	73%*

5	<30% presented fever, fatigue, or cough	No	KPS	Improved*
			CTC in blood	Decreased*
6	Fever, pain cough, fatigue	No	RR	63%*
			ODCR	83%*
			KPS	89.1%*
			QOL	Improved
7	NR	Yes, 1 px by COVID	RECIST	50% SD; 50% PD
			Trafficking and recognition of tumor	Yes*
8	NR	Yes,	OS	15.5 months*
			PFS	6.5months*
			Tumoral markers	Decreased
			ORR	36.4*
			RECIST	NR
9	hypoalbuminemia (45%), hypothyroidism (25%), anemia (20%), hyperglycemia (20%), and hyponatremia (20%)	No	ORR	45%
			OS	17.7 months
			PFS	11.6 months
			RECIST	5% CR; 40% PR
10	NR	No	PFS	Improved*
			RECIST	6.2% CR; 6.2% PR; 12.5% SD; 6.2% PD
			QOL	No changes
11	Acute pain and pneumonia (2 patients)	No	OS	2 years, 58%*
			PFS	33%*
12	hyperglycemia, hypertriglyceridemia, creatine kinase increased, white blood cell decreased, and neutrophil count decreased.	Yes	OS	27.3 months*
			PFS	11.7 months

13	NR	No	Size of tumor and metastasis	Reduction*
14	NR	No	RECIST	NR
			Blood test	Improved
			Size of tumor	Reduction
			Immunophenotyping of lymphocytes	Improved
15	No	No	QOL	Improved
			RECIST	100% CR
16	Nausea, fatigue, fever	No	Lymphocyte count	Increased
			CTC in blood	Decreased in allogeneic group*
			RECIST	Improved in allogeneic group*
			Tumoral markers	Decreased in allogeneic group*
			QOL	Improved in allogeneic group*
17	NR	NR	NK function	Decreased in patients with cancer*
18	Bone marrow suppression, nausea, vomiting, fever	NR	OS	72.5%*
			PFS	51.1%*
			RECIST	NR
19	No	Yes	Lymphocyte count	No changes
			Tumoral markers	No changes
			OS	58 months
20	No	No	QOL	Improved

OS: Overall survival; QOL: Quality of life; RECIST: Response Evaluation Criteria in Solid Tumors (CR: Complete response, PR: Partial response, SD: Stable disease, PD: Progressive disease); PFS: Progression free survival; CTC: Circulant tumoral cells; KPS: Karnofsky performance status; ODCR: Overall disease control rate; ORR: Objective response rate; *: Statistically significance after the treatment, or compared to control group.

Table 3: Efficacy of NK cell therapy in solid tumors.

The heterogeneity observed among the included studies further suggests that therapeutic efficacy is influenced by multiple biological and methodological factors. Among these, the immunosuppressive tumor microenvironment remains one of the principal barriers limiting NK cell infiltration and cytotoxic activity [52]. Likewise, the only study directly comparing autologous and allogeneic NK cells reported superior outcomes for the allogeneic approach, possibly reflecting the enhanced functional capacity of NK cells obtained from healthy donors [59]. Nevertheless, the currently available evidence remains insufficient to establish definitive conclusions regarding the superiority of one therapeutic strategy over another, making this an important area for future investigation.

In addition to their encouraging efficacy, NK cell therapies demonstrated an overall favorable safety profile, with most reported adverse events being mild or moderate and severe toxicities occurring infrequently [56]. However, these findings should be interpreted cautiously given the substantial methodological heterogeneity across studies, including differences in cancer types, cell manufacturing protocols, therapeutic combinations, and outcome assessment methods. Moreover, the predominance of relatively small patient cohorts further limits the statistical strength and generalizability of the available evidence.

Taken together, the findings of this systematic review suggest that the principal challenge facing NK cell therapy is no longer demonstrating its therapeutic potential, but rather achieving methodological standardization. The consistently favorable clinical outcomes observed across different studies indicate that NK cell-based immunotherapy has considerable promise for the treatment of solid tumors. Nevertheless, harmonization of manufacturing procedures, dosing strategies, clinical endpoints, and reporting standards will be essential to generate more robust evidence, facilitate comparisons across clinical trials, and ultimately support the incorporation of NK cell therapies into routine oncological practice.

An important limitation of this systematic review is the limited number of eligible studies identified after the screening process, with only 20 publications fulfilling all predefined inclusion criteria. Furthermore, the available evidence was highly unbalanced across tumor types, as most studies investigated non-small cell lung cancer, whereas breast and colorectal cancers remained underrepresented. This imbalance reflects the current state of clinical research rather than the study design itself and limits the possibility of drawing equally robust conclusions for each malignancy. Therefore, while the present review provides a comprehensive overview of NK cell therapy across selected solid tumors, future disease-specific systematic reviews and meta-analyses will be essential to determine the clinical efficacy of NK cell therapy within each individual cancer type.

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References

1. de Visser KE, Joyce JA. (2023) The evolving tumor microenvironment: From cancer initiation to metastatic outgrowth. Cancer Cell. 41: 374-403.
2. George S. (2024) Carcinogenesis: Exploring the Diverse Mechanisms behind Cancer Development. J Epigenetics Res. 6: 183.
3. WHO. (2024) Global cancer burden growing, amidst mounting need for services. Saudi Med J. 45: 326-327.
4. Silveira FM, Wysocki AD, Mendez RD, Pena SB, Santos EM, et al. (2021) Impact of chemotherapy treatment on the quality of life of patients with cancer. Acta Paul Enferm. 34: eAPE00583.
5. Albarrán-Fernández V, Angelats L, Delgado J, Gros A, Urbano-Ispizua Á, et al. (2025) Unlocking the potential of engineered immune cell therapy for solid tumors. Nat Commun. 16:1144.
6. Shen Z, Meng X, Rautela J, Chopin M, Huntington ND, Et al. (2025) Adjusting the scope of natural killer cells in cancer therapy. Cell Mol Immunol. 22: 699-711.
7. Martín de Civetta MT, Civetta JD. (2011) Carcinogénesis. Salud Publica Mex. 53: 405-14.
8. Singh SR, Bhaskar R, Ghosh S, Yarlagadda B, Singh KK, et al. (2025) Exploring the genetic orchestra of cancer: the interplay between oncogenes and tumor-suppressor genes. Cancers (Basel). 17: 1082.
9. Hanahan D. (2022) Hallmarks of cancer: new dimensions. Cancer Discov. 12: 31-46.
10. Gourmet L, Sottoriva A, Walker-Samuel S, Secrier M, Zapata L, et al. (2024) Immune evasion impacts the landscape of driver genes during cancer evolution. Genome Biol. 25: 168.
11. Brown JS, Amend SR, Austin RH, Gatenby RA, Hammarlund EU, et al. (2023) Updating the definition of cancer. Mol Cancer Res. 21: 1142-7.
12. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A, et al. (2025) Cancer statistics, 2025. CA Cancer J Clin. 75: 10-45.
13. Racacho KJ, Shiau YP, Villa R, Mahri S, Tang M, et al. (2025) The tumor immune microenvironment: implications for cancer immunotherapy, treatment strategies, and monitoring approaches. Front Immunol. 16: 1621812.
14. Marjanovic ND, Hofree M, Chan JE, Canner D, Wu K, et al. (2020) Emergence of a high-plasticity cell state during lung cancer evolution. Cancer Cell. 38: 229-46. e13.
15. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, et al. (2021) Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 71: 209-49.
16. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, et al. (2024) Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 74: 229-63.

17. Anand S, Chan T, Hasan T, Maytin E. (2021) Current prospects for treatment of solid tumors via photodynamic, photothermal, or ionizing radiation therapies combined with immune checkpoint inhibition: a review. Pharmaceuticals (Basel). 14: 447.

18. Liu B, Zhou H, Tan L, Siu KTH, Guan XY, et al. (2024) Exploring treatment options in cancer: tumor treatment strategies. Signal Transduct Target Ther. 9: 175.

19. Nogueira LM, Schafer EJ, Fan Q, Wagle NS, Zhao J, et al. (2024) Assessment of changes in cancer treatment during the first year of the COVID-19 pandemic in the US. JAMA Oncol. 10: 109-17.

20. Truong NTH, Gargett T, Brown MP, Ebert LM. (2021) Effects of chemotherapy agents on circulating leukocyte populations: potential implications for the success of CAR-T cell therapies. Cancers (Basel). 13: 2225.

21. Wang AX, Ong XJ, D'Souza C, Neeson PJ, Zhu JJ, et al. (2023) Combining chemotherapy with CAR-T cell therapy in treating solid tumors. Front Immunol. 14: 1140541.

22. Falk-Mahapatra R, Gollnick SO. (2020) Photodynamic therapy and immunity: an update. Photochem Photobiol. 96: 550-559.

23. Cramer GM, Moon EK, Cengel KA, Busch TM. (2020) Photodynamic therapy and immune checkpoint blockade. Photochem Photobiol. 96: 954-61.

24. Hernández-Idarraga KJ, Arias-Rozo AJ, Arango-Rodríguez ML, Sossa CL, Becerra-Bayona SM, et al. (2026) CAR T-cells in hematologic malignancies: advances, challenges, and future directions. iScience. 29: 115213.

25. Klingemann H. (2023) The NK-92 cell line—30 years later: its impact on natural killer cell research and treatment of cancer. Cytotherapy. 25: 451-457.

26. Alieva M, van Rheenen J, Broekman MLD. (2018) Potential impact of invasive surgical procedures on primary tumor growth and metastasis. Clin Exp Metastasis. 35: 319-31.

27. Peng L, Sferruzza G, Yang L, Zhou L, Chen S, et al. (2024) CAR-T and CAR-NK as cellular cancer immunotherapy for solid tumors. Cell Mol Immunol. 21: 1089-108.

28. Jørgensen LV, Christensen EB, Barnkob MB, Barington T. (2025) The clinical landscape of CAR NK cells. Exp Hematol Oncol. 14: 46.

29. Zhong Y, Liu J. (2024) Emerging roles of CAR-NK cell therapies in tumor immunotherapy: current status and future directions. Cell Death Discov. 10.

30. Zhang G, Zhao H, Wu J, Li J, Xiang Y, et al. (2014) Adoptive immunotherapy for non-small cell lung cancer by NK and cytotoxic T lymphocytes mixed effector cells: retrospective clinical observation. Int Immunopharmacol. 21: 396-405.

31. Nguyen TMT, Van Tran K, Ta VT, Tran LM, Tran CK, et al. (2022) A case of response to combination treatment with autologous immunotherapy and bevacizumab in advanced non-small cell lung cancer. Respir Med Case Rep. 42: 101804.

32. Iliopoulou EG, Kountourakis P, Karamouzis MV, Doufexis D, Ardavanis A, et al. (2010) A phase I trial of adoptive transfer of allogeneic natural killer cells in patients with advanced nonsmall cell lung cancer. Cancer Immunol Immunother. 59: 1781-9.

33. Yang YJ, Park JC, Kim HK, Kang JH, Park SY, et al. (2013) A trial of autologous ex vivo-expanded NK cell-enriched lymphocytes with docetaxel in patients with advanced non-small-cell lung cancer as second- or third-line treatment: phase IIa study. Anticancer Res. 33: 2115-22.

34. Lin M, Liang S, Shi J, Niu L, Chen J, et al. (2017) Circulating tumor cell as a biomarker for evaluating allogenic NK cell immunotherapy on stage IV non-small cell lung cancer. Immunol Lett. 191: 10-15.

35. Lin M, Liang SZ, Wang XH, Liang YQ, Zhang MJ, et al. (2017) Clinical efficacy of percutaneous cryoablation combined with allogenic NK cell immunotherapy for advanced non-small cell lung cancer. Immunol Res. 65: 880-7.

36. Villalona-Calero MA, Tian L, Li X, Palmer JM, Aceves C, et al. (2025) Interim report on engineered NK cell trial in lung cancer refractory to immune checkpoint inhibitors. JCI Insight. 10: e186890.

37. Wang Z, Zhang R, Cao Y, Chen Y, Huang S, et al. (2023) Investigation of the efficacy and feasibility of combined therapy of PD-L1-enhanced exogenous peripatetic adoptive natural killer (NK) cells in combination with antiangiogenic targeted therapy in the treatment of extensive-stage small cell lung cancer. Thorac Cancer. 14: 2877-2885.

38. Lin M, Luo H, Liang S, Chen J, Liu A, et al. (2020) Pembrolizumab plus allogeneic NK cells in advanced non-small cell lung cancer patients. J Clin Invest. 130: 2560-2569.

39. Kokowski K, Stangl S, Seier S, Hildebrandt M, Vaupel P, et al. (2019) Radiochemotherapy combined with NK cell transfer followed by second-line PD-1 inhibition in a patient with NSCLC stage IIIb inducing long-term tumor control: a case study. Strahlenther Onkol. 195: 352-361.

40. Jia L, Chen N, Chen X, Niu C, Liu Z, et al. (2022) Sintilimab plus autologous NK cells as second-line treatment for advanced non-small-cell lung cancer previously treated with platinum-containing chemotherapy. Front Immunol. 13: 1074906.

41. Multhoff G, Seier S, Stangl S, Sievert W, Shevtsov M, et al. (2020) Targeted natural killer cell-based adoptive immunotherapy for the treatment of patients with NSCLC after radiochemotherapy: a randomized phase II clinical trial. Clin Cancer Res. 26: 5368-5379.

42. Park HJ, Kim YM, Jung JS, Ji W, Lee JC, et al. (2022) Two-year efficacy of SNK01 plus pembrolizumab for non-small cell lung cancer: expanded observations from a phase I/IIa randomized controlled trial. Thorac Cancer. 13: 2050-2056.

43. Jia L, Chen N, Chen X, Niu C, Liu Z, et al. (2025) Updated overall survival data and predictive biomarkers of autologous NK cells plus sintilimab as second-line treatment for advanced non-small cell lung cancer. Front Immunol. 16: 1595382.

44. Chidambaram R, Terunuma H, Balamurugan M, Dedeepiya VD, Sumana P, et al. (2017) Cell-based immunotherapy in stage IIIA inflammatory breast cancer with declining innate immunity following successive chemotherapies: a case report. Mol Clin Oncol. 7: 493-497.

45. Liang S, Xu K, Niu L, Wang X, Liang Y, et al. (2017) Comparison of autogeneic and allogeneic natural killer cells immunotherapy on the clinical outcome of recurrent breast cancer. Onco Targets Ther. 10: 4273-4281.

46. Mamessier E, Sylvain A, Thibult M, Houvenaeghel G, Jacquemier J, et al. (2011) Human breast cancer cells enhance selfTolerance by promoting evasion from NK cell antitumor immunity. J Clin Invest. 121: 3609-3622.

47. Li L, Li W, Wang C, Yan X, Wang Y, et al. (2018) Adoptive transfer of natural killer cells in combination with chemotherapy improves outcomes of patients with locally advanced colon carcinoma. Cytotherapy. 20:134-148.

48. Milani V, Stangl S, Issels R, Gehrmann M, Wagner B, et al. (2009) Anti-tumor activity of patient-derived NK cells after cell-based immunotherapy: a case report. J Transl Med. 7: 50.

49. Bagus BI. (2023) Autologous natural killer cells as a promising immunotherapy for locally advanced colon adenocarcinoma: three years follow-up of a resectable case. Cancer Rep (Hoboken). 6: e1866.

50. Vivier E, Rebuffet L, Narni-Mancinelli E, Cornen S, Igarashi RY, et al. (2024) Natural killer cell therapies. Nature. 626: 727-736.

51. Lamers Kok N, Panella D,Georgoudaki AM,Liu H,Özkazanc D, et al. (2022) Natural killer cells in clinical development as non-engineered, engineered, and combination therapies. J Hematol Oncol. 15:164.

52. Tong L, Jiménez-Cortegana C, Tay APHM, Wickström S, Galluzzi L, et al. (2022) NK cells and solid tumors: therapeutic potential and persisting obstacles. Mol Cancer. 21: 206.

53. Chu J, Gao F, Yan M, Zhao S, Yan Z, et al. (2022) Natural killer cells: a promising immunotherapy for cancer. J Transl Med. 20: 240.

54. Kim N, Yi E, Lee E, Park HJ, Kim HS, et al. (2024) Interleukin-2 is required for NKp30-dependent NK cell cytotoxicity by preferentially regulating NKp30 expression. Front Immunol. 15: 1388018.

55. Habif G, Crinier A, André P, Vivier E, Narni-Mancinelli E, et al. (2019) Targeting natural killer cells in solid tumors. Cell Mol Immunol. 16: 415-422.

56. Park H, Kim G, Kim N, Ha S,Yim H, et al. (2024) Efficacy and safety of natural killer cell therapy in patients with solid tumors: a systematic review and meta-analysis. Front Immunol. 15: 1454427.

57. Wolchok JD, Hoos A, O'Day S, Weber JS, Hamid O, et al. (2009) Guidelines for the evaluation of immune therapy activity in solid tumors: immune-related response criteria. Clin Cancer Res. 15: 7412-7420.

58. Seymour L, Bogaerts J, Perrone A, Ford R, Schwartz LH, et al. (2017) iRECIST: guidelines for response criteria for use in trials testing immunotherapeutics. Lancet Oncol. 18: e143-e152.

59. Yang Y, Lim O, Kim TM, Ahn YO, Choi H, et al. (2016) Phase I study of random healthy donor-derived allogeneic natural killer cell therapy in patients with malignant lymphoma or advanced solid tumors. Cancer Immunol Res. 4: 215-224.