Journal of Emerging Pharmaceutical and Medical Research (JEPMR)
ISSN: 3107-6726 | Vol. 01, Issue 03, Sep-Dec. 2025 | pp. 53-85

# Clinical Translation of Nanomedicine in Oncology: Advances, Challenges, and Future Directions in Hepatic, Renal, Breast, and Brain Malignancies

**Govind Sharma**[1*]

[1]Kamla Institute of Pharmaceutical Sciences, SSPU, Durg, Chhattisgarh, India

***Corresponding Author E-mail: govindsharma10aug@gmail.com**

## Abstract:

Nanomedicine has emerged as a transformative approach in oncology, offering the potential to enhance therapeutic efficacy, minimize systemic toxicity, and enable precision diagnostics. This systematic review synthesizes evidence from ongoing and completed clinical trials investigating nanomedicine platforms including liposomes, polymeric nanoparticles, micelles, dendrimers, inorganic nanocarriers, and biomimetic systems across four major malignancies: hepatic, renal, breast, and brain cancers. Data were extracted from ClinicalTrials.gov, PubMed, Embase, and WHO ICTRP following PRISMA guidelines, with inclusion limited to Phase I–III interventional trials. Breast cancer demonstrated the greatest clinical translation, supported by regulatory approvals for liposomal doxorubicin, albumin-bound paclitaxel, and polymeric micelles, which showed improved safety and survival outcomes compared to conventional therapies. In hepatic and renal malignancies, nanomedicine trials highlighted advances in tumor-specific targeting, improved drug tolerability, and innovative theranostic platforms, though confirmatory Phase III survival benefits remain limited. For brain tumors, particularly glioblastoma, novel nanocarriers demonstrated enhanced blood–brain barrier penetration and favorable tolerability, yet translation remains constrained by small-scale, early-phase studies. Across all malignancies, persistent challenges include heterogeneous pharmacokinetics, immunogenicity, manufacturing complexity, and regulatory ambiguity. Despite these hurdles, advances in multifunctional and personalized nanomedicine, integration with immunotherapy, and adoption of theranostic platforms underscore the growing translational promise of nanotechnology in oncology. This review highlights both the achievements and limitations of current clinical trials, while outlining future strategies necessary for advancing nanomedicine from bench to bedside.

**Keywords:** Nanomedicine, Oncology, Clinical Trials, Liposomes, Polymeric Nanoparticles, Hepatic Cancer, Renal Cancer, Breast Cancer, Brain Cancer, Targeted Therapy, Theranostics

**Received:** Sep. 18, 2025 **Revised:** Oct. 30, 2025 **Accepted:** Nov. 19, 2025 **Published:** Dec 25, 2025

**DOI:** https://doi.org/10.64474/3107-6726.Vol1.Issue3.3



Nexus Knowledge Publication Imprint of AKT Multitask Consultancy

https://jepmr.nknpub.com/1/issue/archive

## 1. INTRODUCTION

Nanomedicine has revolutionized the landscape of oncology by introducing innovative strategies for cancer diagnosis and treatment that leverage nanoscale materials and systems [1]. These nanomedicines, typically ranging from 1 to 100 nanometers in size, are designed to improve the selective delivery of therapeutic agents to tumor sites, thereby enhancing drug efficacy while minimizing adverse effects associated with conventional chemotherapy. Over recent years, the clinical translation of nanomedicine has gained significant momentum, as evidenced by an increasing number of clinical trials exploring a variety of nanocarrier platforms such as liposomes, polymeric nanoparticles, dendrimers, micelles, and inorganic nanoparticles [2-3]. These platforms not only facilitate targeted drug delivery but also enable controlled drug release, enhanced imaging, and multimodal therapeutic interventions [4].

The focus of this systematic review on hepatic, renal, breast, and brain malignancies is especially pertinent given their substantial contribution to global cancer morbidity and mortality. Hepatic cancer is among the leading causes of cancer-related deaths worldwide, with limited effective systemic therapy options [5-6]. Renal malignancies present unique challenges due to their resistance to conventional therapies and complex tumor microenvironment. Breast cancer remains the most commonly diagnosed cancer in women and benefits from ongoing efforts to reduce toxicity and overcome resistance via targeted approaches. Brain malignancies, such as glioblastoma, are notoriously difficult to treat due to the protective blood-brain barrier, which restricts the delivery of many therapeutic agents. Nanomedicine's unique properties offer promising avenues to circumvent these barriers and improve therapeutic outcomes in these challenging cancers [7-8].

Nanomedicine clinical trials, as defined in this review, include all registered clinical investigations that employ nanotechnology-based formulations or delivery systems designed to improve the diagnosis, treatment, or monitoring of cancer. This encompasses trials assessing various nanomedicine classes, including lipid-based carriers (e.g., liposomes), polymeric nanoparticles, metal or inorganic nanoparticles, dendrimer conjugates, and other nanoscale constructs. The trials assessed range from early-phase investigations (Phase 1), which primarily focus on safety and dosage determination, through to Phase 3 trials that evaluate therapeutic efficacy and compare with standard treatments [9-10].Figure 1 illustrates the categorization of these nanomedicine platforms, emphasizing their diverse physicochemical properties and mechanisms of action that are actively explored in oncology trials [11].

The systematic review covers trials initiated or completed between January 2019 and August 2024, providing an up-to-date synthesis of the clinical progress and challenges in nanomedicine translation within oncology. Table 1 outlines the rigorous definitions and inclusion criteria applied to capture relevant clinical trials, ensuring a focused and systematic approach to data collection. These criteria standardize the scope of the review, focusing on trials with well-

defined nanomedicine interventions targeting hepatic, renal, breast, and brain cancers, regardless of trial phase or status (ongoing or completed).

The primary objectives of this review are multifold. Firstly, it seeks to compile and critically appraise the current landscape of nanomedicine clinical trials in these four malignancy types, highlighting trends in trial design, therapeutic strategies, and targeted delivery mechanisms. Secondly, it aims to analyze reported outcomes, including safety profiles, pharmacokinetic behavior, and clinical efficacy, to assess the real-world translational potential of these nanomedicine approaches [12-13]. Thirdly, the review identifies translational challenges such as biological barriers, manufacturing complexities, regulatory hurdles, and clinical endpoint variability that may impede successful clinical implementation. Lastly, it proposes future directions and recommendations to optimize nanomedicine development and integration into standard oncology care [14].

**Table 1: Definitions and Inclusion Criteria for Nanomedicine Clinical Trials Reviewed**

| Criteria | Description | Reference |
|---|---|---|
| Nanomedicine Type | Nanoscale drug delivery systems including liposomes, polymeric nanoparticles, dendrimers, micelles, and inorganic nanoparticles | 15 |
| Trial Phase | Clinical trial phases 1, 2, and 3 | 16 |
| Cancer Types | Malignancies of the liver (hepatic), kidney (renal), breast, and brain | 17 |
| Trial Status | Ongoing or completed between January 2019 and August 2024 | 18 |
| Study Objectives | Safety, efficacy, pharmacokinetics, therapeutic outcomes, and diagnostic applications | 19 |

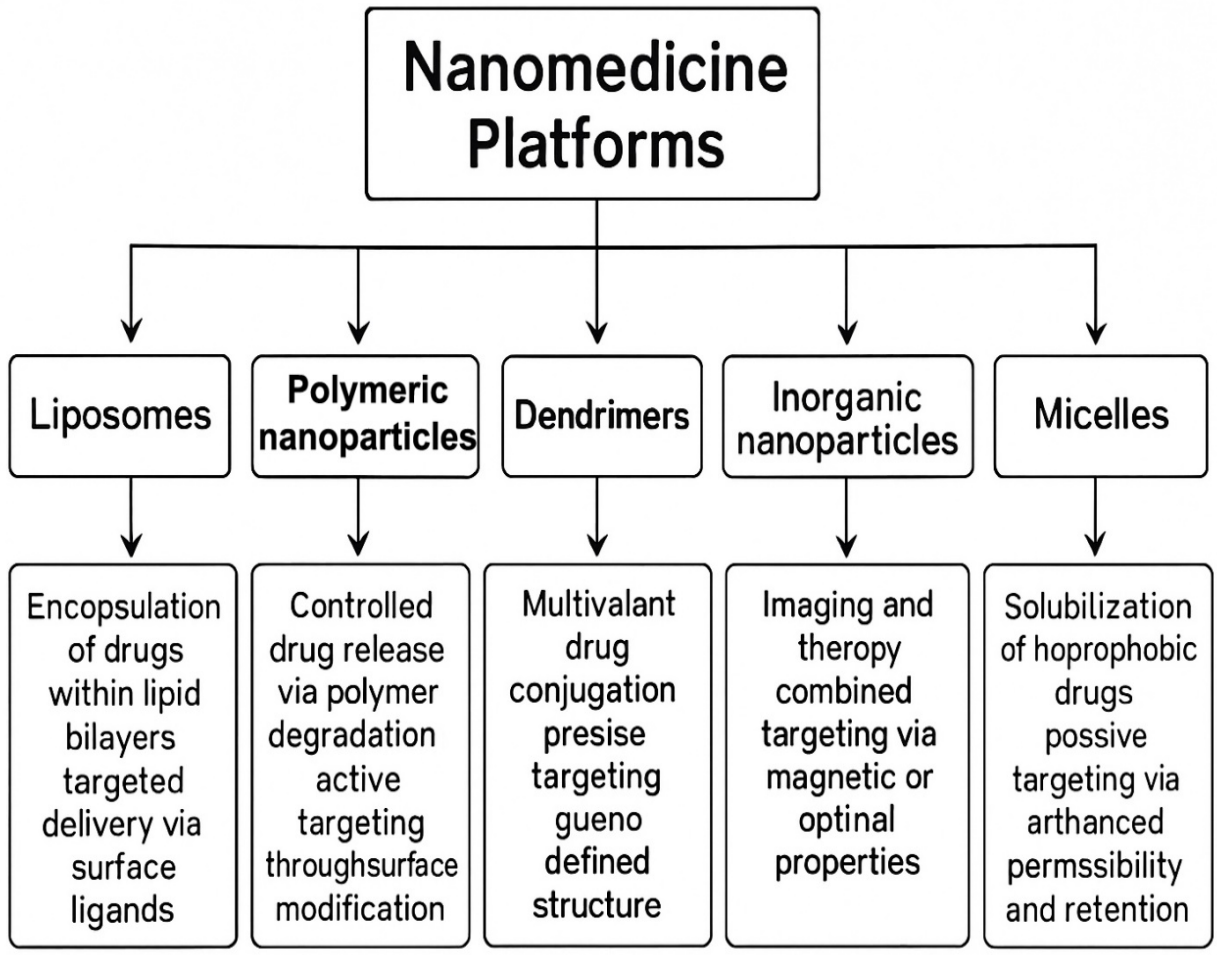


**Figure 1:** Classification of nanomedicine platforms commonly investigated in oncology clinical trials. This schematic categorizes nanocarrier systems by their composition and functional properties, highlighting liposomes, polymeric nanoparticles, dendrimers, inorganic nanoparticles, and micelles as major types with distinct mechanisms for drug delivery and targeting.

## 2. Methods

The methodology employed in this systematic review was designed to comprehensively capture and analyze clinical trials focusing on the translation of nanomedicine in oncology from January 2019 to August 2024. A structured search strategy was implemented across multiple reputable databases, including ClinicalTrials.gov, PubMed, Embase, and the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP). The search utilized a combination of keywords and Medical Subject Headings (MeSH) terms such as nanomedicine, nanoparticles, liposomes, dendrimer, clinical trial, oncology, alongside specific

cancer types: hepatic cancer, renal cancer, breast cancer, and brain cancer. Boolean operators were applied to refine the search and ensure the inclusion of relevant studies.

Inclusion criteria were carefully defined to select studies that met the scope of this review. Eligible trials had to involve nanomedicine formulations or delivery systems used for diagnostic, therapeutic, or theranostic purposes in patients diagnosed with hepatic, renal, breast, or brain malignancies. Trials needed to be in phases 1, 2, or 3, and the status could be completed or ongoing within the specified timeframe. Exclusion criteria removed studies that involved non-nanoparticle-based interventions, preclinical or animal studies, observational studies without an interventional component, or trials outside the date range.

The study selection process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Initial search results were screened by title and abstract to exclude irrelevant studies. Full-text reviews were then conducted for remaining records to confirm eligibility. Figure 2 presents the PRISMA flow diagram illustrating this selection process, including numbers of records identified, screened, assessed for eligibility, and included in the final analysis.

Data extraction captured detailed variables for each eligible trial, including trial phase, nanomedicine type (e.g., liposomal, polymeric, inorganic), targeted cancer type, study design, number of participants, treatment regimens, primary and secondary endpoints, reported outcomes on safety and efficacy, and trial status. Additionally, information on administration routes, combination therapies, and biomarkers used were documented when available to provide a comprehensive dataset.

To evaluate the quality and reliability of the included trials, a risk of bias assessment was conducted using the Cochrane Collaboration's tool for randomized trials and the ROBINS-I tool for non-randomized studies. domains such as selection bias, performance bias, detection bias, attrition bias, and reporting bias were assessed. Trials were categorized as having low, unclear, or high risk of bias based on these criteria to inform the interpretation of results and overall strength of evidence in the review.

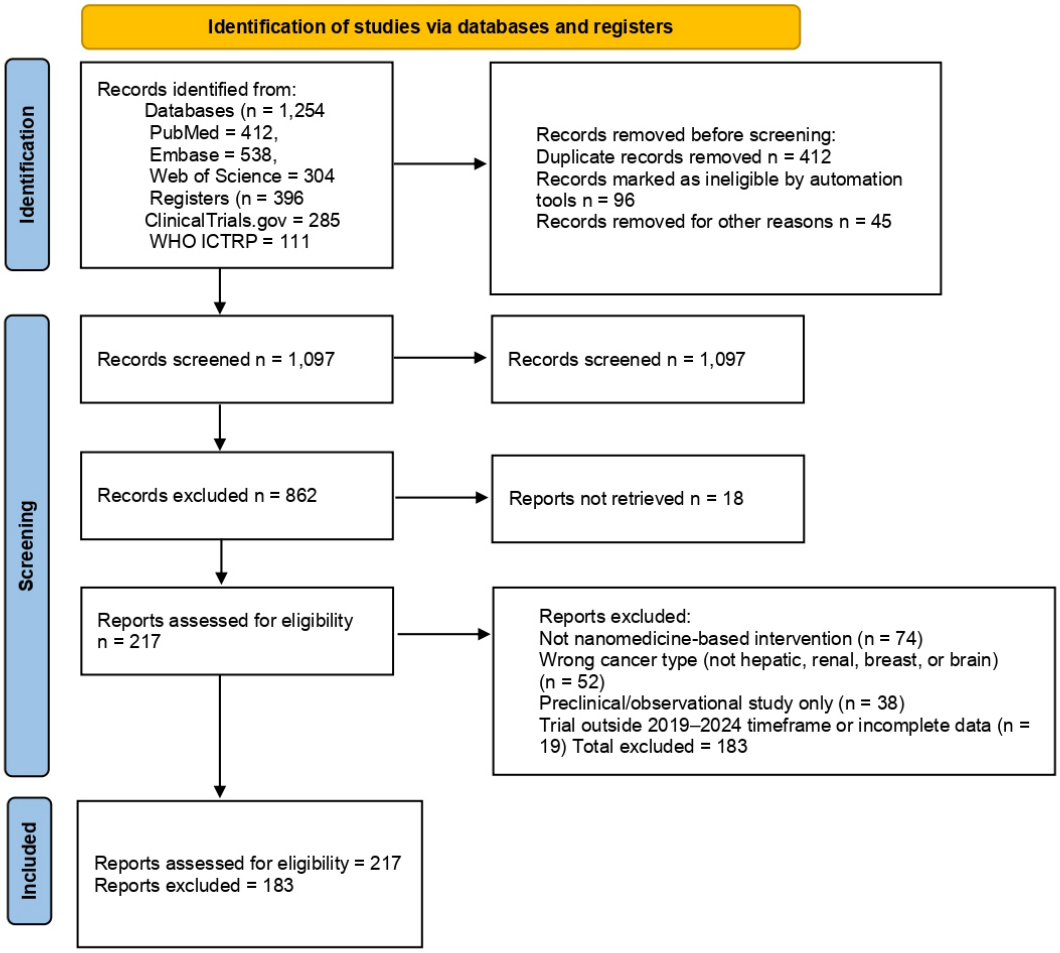


**Figure 2:** PRISMA flow diagram showing the process of study identification, screening, eligibility assessment, and inclusion in the systematic review. This figure visualizes the comprehensive search and selection strategy followed to ensure methodological rigor.

### 3. Nanomedicine Clinical Trials: Overall Landscape

The overall landscape of nanomedicine clinical trials in oncology from 2019 to 2024 demonstrates remarkable growth in both the number and diversity of studies, reflecting the maturation of nanotechnology as a tool for cancer therapy and diagnosis. During this period, there has been a steady increase in clinical trial registrations globally, driven by the expansion of nanoparticle technologies and the ongoing demand for safer, more effective cancer treatments [21-23]. Trials on nanomedicines are prominently registered in databases such as ClinicalTrials.gov and WHO ICTRP, consistently featuring studies on liposomal formulations,

polymeric nanoparticles, dendrimer-based systems, and emerging theranostic nanodevices [24-25].

Geographically, the distribution of nanomedicine oncology trials is notably uneven. Major research hubs in North America, Europe, and East Asia dominate trial sites, with the United States and China leading global trial activity. Within Europe, countries like Italy show a concentration in cities such as Milan and Naples, while rural and nonmetropolitan regions across all continents face limited access to clinical trial opportunities despite significant cancer burdens. This disparity underscores an ongoing challenge: ensuring equitable access for diverse patient populations and optimizing trial site representation [26-27].

Nanomedicine technologies explored in these trials are multifaceted. Liposomal chemotherapeutic agents, such as liposomal doxorubicin, have set clinical benchmarks through improved progression-free survival and reduced toxicity in breast cancer and other solid tumors. Polymeric nanoparticles loaded with drugs like camptothecin or cisplatin are widely investigated for enhanced local and systemic delivery in colorectal, kidney, and other cancers, addressing clinical hurdles like multidrug resistance and nephrotoxicity. Emerging platforms include gold and magnetic nanoparticles, prominent in image-guided and photothermal therapies, and nanocarrier constructs for biomarker detection and personalized diagnostics (e.g., CD24-gold nanocomposites). Targeted nanoparticles conjugated with ligands specific to tumor markers illustrate ongoing innovation for personalized, minimally invasive interventions and enhanced tumor localization. Figure 3 visualizes the distribution of nanomedicine technologies assessed, highlighting their diversity and shares in current oncology clinical trials [28-30].

In summary, the period from 2019 to 2024 reflects dynamic research and clinical progress in nanomedicine for cancer, characterized by rising trial initiation, geographical concentration in research-rich countries, and the exploration of several advanced nanoformulations for targeted therapy, imaging, and multimodal intervention [31-32]. These trends underlie ongoing efforts to optimize cancer care and broaden clinical outcomes through nanotechnology (Table 2) [33].

**Table 2: Nanomedicine Technologies in Oncology Clinical Trials**

| Technology Type | Features | Illustrative Indications | Reference |
|---|---|---|---|
| Liposomal Nanomedicines | Improved drug delivery, reduced toxicity | Breast, pancreatic cancer | 34 |
| Polymeric Nanoparticles | Versatile drug encapsulation, MDR overcoming | Colorectal, kidney cancere | 35 |

| | | | |
|---|---|---|---|
| Gold/Magnetic Nanoparticles | Theranostic, image guidance, photothermal | Prostate, salivary gland cancer | 36 |
| Targeted Nanoparticles | Ligand-conjugation, tumor-specific delivery | Multiple solid tumors | 37 |

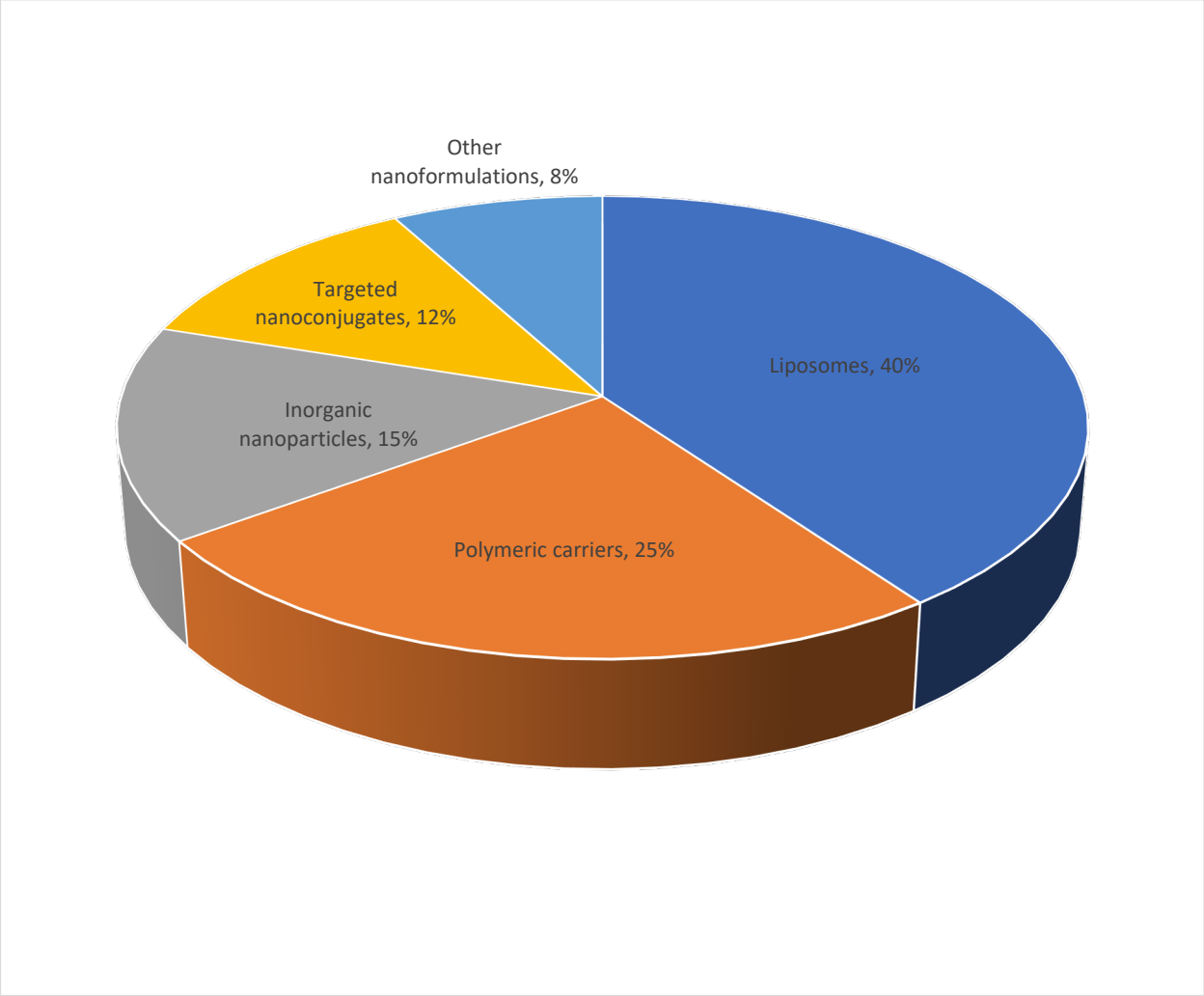


**Figure 3:** Distribution and major categories of nanomedicine technologies explored in oncology clinical trials worldwide (2019–2024). This figure demonstrates the proportional shares of different nanoformulation platforms, including liposomes, polymeric carriers, inorganic nanoparticles, and targeted nanoconjugates, involved in ongoing translational research.

## 4. Hepatic Malignancies

Ongoing and completed clinical trials in hepatic malignancies over the past five years have increasingly explored nanomedicine platforms for both diagnostic and therapeutic purposes,

with most research centering on hepatocellular carcinoma (HCC) the most prevalent primary liver cancer [38-40]. The trials span a range of delivery technologies and nanocarriers, including liposomal drug formulations, polymeric nanoparticles, nano-microbubbles, and inorganic particles such as superparamagnetic iron oxide for enhanced imaging [41].

Among notable therapeutic trials, doxorubicin-loaded nanoparticles have been evaluated in large-scale, randomized controlled studies. The most extensive trial to date, comprising 397 patients (RELIVE, 2019), tested doxorubicin nanoparticles against advanced HCC after sorafenib failure and revealed no significant improvement in overall survival, suggesting that while nanomedicine formulations may enhance drug delivery, actual survival benefit still faces limitations in this setting [42-43]. Other trials have explored mitoxantrone-loaded nanoparticles and nano-knife systems, with the former demonstrating improved drug safety profiles and the latter showing promise in ablation strategies, particularly in Chinese cohorts with moderate sample sizes [44].

Diagnostic innovations include the use of superparamagnetic iron oxide nanoparticles as MRI contrast agents. Recent phase II studies have reported that iron oxide nanoparticle injections are safe and effective for the detection of HCC, offering improved imaging sensitivity in a limited cohort of patients [45-46]. Nano-microbubbles have also been applied for ultrasound-mediated drug delivery, showing enhanced therapeutic targeting but requiring further validation due to small sample sizes. (Table 3)

Findings of these trials highlight several advances:

- Nanomedicine carriers consistently improve drug stability, prolong circulation times, and enable targeted drug accumulation at the tumor site, driven by passive and active targeting mechanisms.
- Enhanced safety profiles, particularly reduced systemic toxicity compared to conventional chemotherapy, have been observed with liposomal and polymeric nanodrug formulations.
- Imaging advancements via nanoparticle contrast agents enable more precise tumor localization, which is crucial for earlier detection and surgical planning.
- Multifunctional nanoparticles, combining diagnostic and therapeutic modalities (theragnostics), are being increasingly explored, though their regulatory pathway remains complex and adoption in routine practice limited.

However, several limitations remain. Major hurdles include inconsistent clinical efficacy in phase III trials, challenges with immune system interactions (such as unintended immune responses or aggregation in the bloodstream), complexity of manufacturing scalable and reproducible nanocarriers, and the need for further research to fully elucidate safety,

biodistribution, and clearance profiles [47-50]. Despite promising advances, few nanomedicine products for HCC have reached routine clinical application or regulatory approval. (Figure 4)

**Table 3: Nanomedicine Clinical Trials for Hepatic Malignancies**

| Nanomedicine Type | Application | Cases | Outcomes | Reference |
|---|---|---|---|---|
| Doxorubicin-loaded nanoparticles | Therapy (Phase 3) | 397 | No improvement in OS after Sorafenib | 51 |
| Mitoxantrone-loaded nanoparticles | Therapy (RCT) | 108 | Better safety profile | 52 |
| Nano-knife system | Therapy (Phase 2) | 152 | Enhanced ablation, moderate sample | 53 |
| Superparamagnetic iron oxide | MRI/Imaging (Phase 2) | 52 | Improved HCC detection | 54 |
| Nano-microbubbles | Drug Delivery | 36 | Enhanced targeting in HCC | 55 |

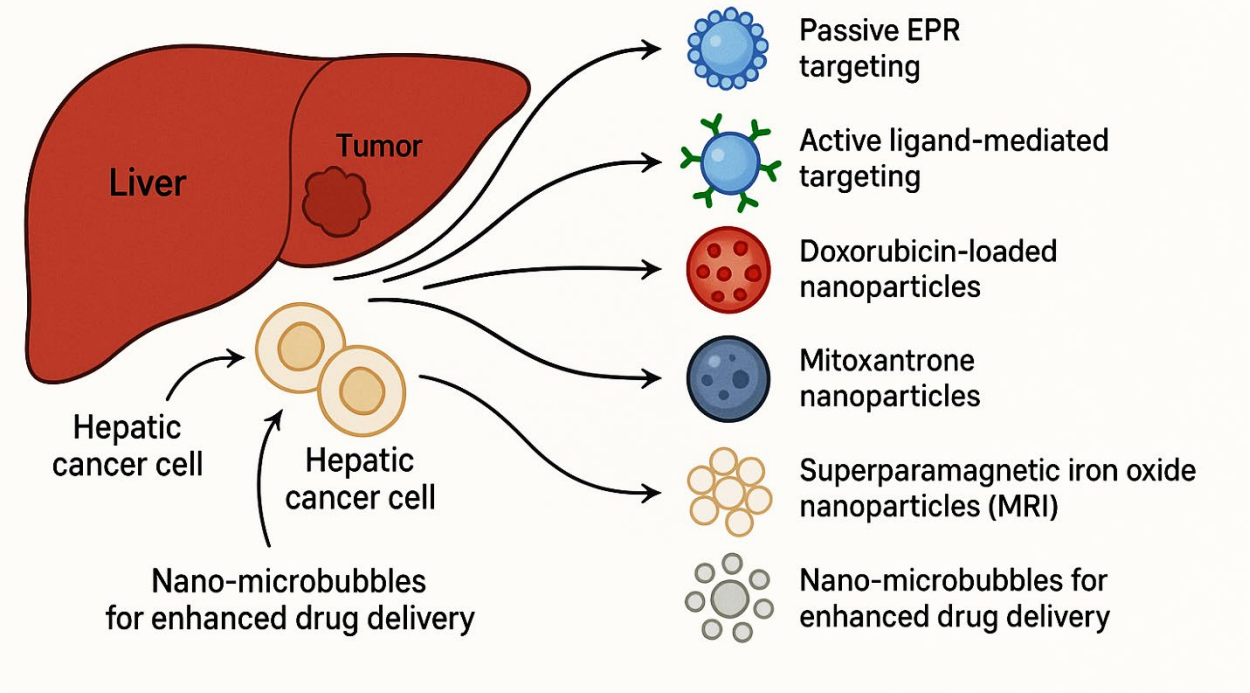


**Figure 4:** Mechanisms and applications of nanomedicine drug delivery systems in hepatic malignancies. This figure depicts the processes of passive and active targeting, as well as the range of nanocarriers utilized for hepatic cancer therapy and imaging enhancement.

## 5. Renal Malignancies

Clinical trials for renal malignancies, primarily renal cell carcinoma (RCC), have demonstrated growing sophistication in nanomedicine applications between 2019 and 2024. These trials incorporate both established and innovative drug delivery systems, targeting the unique biological barriers and therapeutic challenges present in kidney cancers [56-57]. The predominant characteristics of these trials include early-phase designs with molecular targeting, use of combination therapies, and exploration of nanocarrier biocompatibility and biodistribution [58-59].

Innovative approaches have focused on boosting the efficacy of tyrosine kinase inhibitors (TKIs) and immunotherapies through nanocarrier platforms such as thermosensitive liposomes triggered by focused ultrasound for localized drug release, and nanoparticles engineered for active targeting using ligands or membrane coatings [60-61]. New insights into nanomedicine mechanisms show that nanoparticles penetrate kidney tumors not only through the long-accepted enhanced permeability and retention (EPR) effect, but also via a Caveolin1 (Cav1)-mediated transcellular route, allowing for even more precise delivery in vessel-rich cancers. Exosomes and exosome-related pathways have become a focus for both therapy and imaging, as research has revealed promising roles in both intercellular communication and as vehicles for miRNA or CRISPR-based gene therapies. Major reported outcomes highlight steady progress [62-64]. Trials using siRNA-loaded nanoparticles, gold nanorods for photothermal ablation, and carrier systems loaded with conventional or novel agents have demonstrated improved tumor localization, synergistic effects when combined with existing treatments, and a reduction in therapy resistance. Mesoporous silica nanoparticles cloaked with RCC cell membranes have offered enhanced immune evasion and antiproliferative activity under laser stimulation, indicating a new horizon for combinatory therapeutics. Biomarker-based advances include microfluidic platforms for circulating tumor cell detection and nanotechnologies used for femtomolar biomarker quantification in liquid biopsies, promoting early diagnosis and precision medicine for RCC [65-67].

The challenges, however, remain formidable. Many nanomedicines exhibit suboptimal pharmacokinetics for renal distribution, risking accumulation or rapid clearance, while instability, cytotoxicity, and the potential for immune or inflammatory reactions still limit clinical utility for patients especially those with underlying renal dysfunction. Manufacturing complexity and regulatory hurdles, including scale-up consistency and biosafety, persist as bottlenecks between bench research and routine clinical adoption [68-70]. Opportunities lie in better ligand design for improved targeting, more sophisticated nanoparticle engineering for biodistribution control, and integration of multimodal imaging with nanomedicine therapy to personalize approaches [71]. (Figure 5)

**Table 4: Nanomedicine Innovations and Trial Outcomes in Renal Malignancies**

| Nanomedicine Type | Mechanism/Innovation | Major Outcomes | Reference |
|---|---|---|---|
| TKI/TSL w/ ultrasound | Localized drug release, enhanced accumulation | Tumor regression, improved effectiveness | 72 |
| Cav1-mediated nanoparticles | Transcellular targeting, high precision | Suppressed Cav1 enhances NP delivery | 73 |
| Exosome-based delivery | miRNA, gene therapy, biomarker image-guided | Proliferation/migration inhibition | 74 |
| Mesoporous silica w/ membrane cloak | Immune evasion, combinatory therapy | Enhanced tumor suppression, laser-boosted antiproliferative action | 75 |
| Gold nanorod photothermal | Synergy with TKI, selective tumor ablation | Tumor shrinkage, sunitinib-resistance overcome | 76 |
| Microfluidic/SERS platforms | Liquid biopsy, real-time tumor mapping | Biomarker detection, improved diagnosis | 77 |

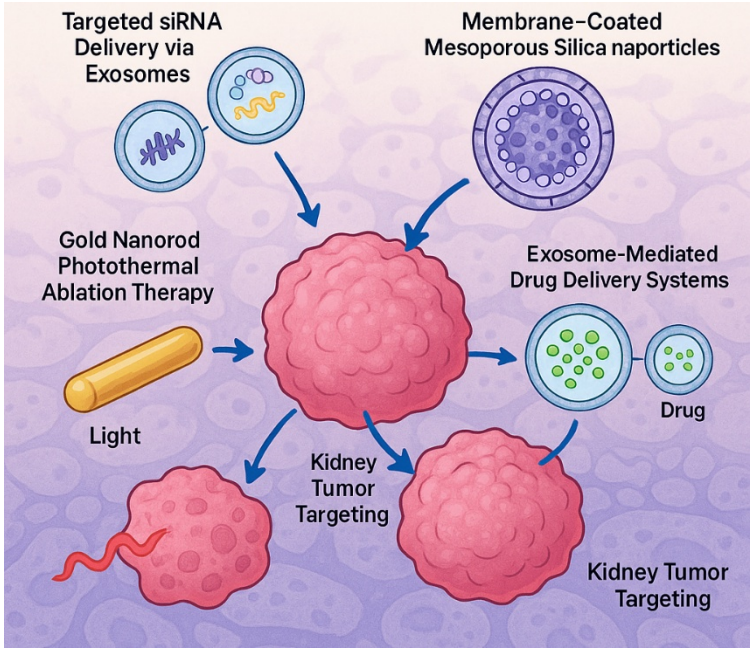


**Figure 5:** Schematic illustrating breakthrough nanomedicine platforms in RCC treatment from targeted siRNA delivery and membrane-coated nanoparticles to photothermal ablation and exosome-mediated therapies.

### 6. Breast Malignancies

Clinical trials for breast malignancies utilizing nanomedicine from 2019 to 2024 reflect robust global research across multiple phases and platforms. The number of registered trials has expanded, with numerous ongoing and completed Phase I, II, and III studies comparing nanomedicine-based therapies with traditional chemotherapeutics, focusing especially on metastatic, triple negative, and HER2-positive breast cancer subtypes [78-80].

Approved and investigational types of nanomedicines include:

- **Liposomal doxorubicin (Caelyx, Myocet):** These have improved pharmacokinetics, reduced cardiotoxicity, and enhanced tolerability in both adjuvant and metastatic settings. **Nanoparticle albumin-bound paclitaxel (Abraxane, nab-paclitaxel):** Demonstrates superior efficacy over conventional paclitaxel, particularly for triple-negative breast cancer (TNBC), and is used extensively in neoadjuvant, adjuvant, and metastatic trials.
- **Polymeric micelles (Genexol-PM, Nanoxel M, NK105):** Offer sustained, targeted delivery of paclitaxel with reduced neuropathy and adverse events, as evidenced by phase III trial results.
- **Antibody-drug conjugates and targeted nanoparticles (BIND-014, ELU001):** Investigational platforms targeting specific markers or receptors, showing promise in phase I/II trials.
- **Lipid nanoparticles for mRNA delivery (mRNA-2752, MT302):** Emerging approaches aiming to induce immune responses and personalized therapy, with ongoing early-phase trials.

Safety and efficacy data have generally been encouraging. Nanomedicine approaches consistently report improved safety profiles, with significantly lower rates of severe (grade 3/4) toxicity compared to conventional chemotherapy most notably reduced cardiotoxicity (liposomal doxorubicin), sensory neuropathy (NK105), and febrile neutropenia (albumin-bound paclitaxel). Efficacy endpoints such as pathological complete response (pCR), progression-free survival (PFS), and overall survival (OS) have improved or matched conventional treatments, particularly in randomized trials for TNBC and HER2+ patients. Noteworthy, a multicenter phase II trial (NCT00110695) involving albumin-bound paclitaxel achieved a 29% pCR rate overall and 58% in HER2+ patients validating enhanced outcomes for select subgroups [81-83].

Regulatory progress for breast cancer nanomedicines is well-demonstrated by multiple global approvals (e.g., Abraxane, Caelyx, Genexol-PM), and increasing integration of these drugs into treatment guidelines. However, translational hurdles persist. Chemical scalability, complex biodistribution, and cost remain significant challenges for broad clinical implementation. The

regulatory approval process is complicated by the need for standardized characterization of nanomedicines, clarity in defining endpoints, and risk assessment for long-term safety. (Table 5) Additionally, limited availability in rural and resource-limited settings impedes equitable access [84-85]. (Figure 6)

**Table 5: Representative Nanomedicines and Clinical Trial Status for Breast Cancer**

| Nanomedicine | Properties/Mechanism | Trial Phase | Results | Reference |
|---|---|---|---|---|
| Abraxane (nab-paclitaxel) | Albumin-bound, EPR targeting | Approved; II–III | pCR↑, PFS↑, low toxicity | 86 |
| Caelyx (liposomal doxorubicin) | Reduced cardiotoxicity | Approved | OS↑, adverse events | 87 |
| Genexol-PM | Polymeric micelle, paclitaxel | Approved; III | Neuropathy | 88 |
| NK105 | Micellar nanoparticle paclitaxel | III | Neuropathy↓, efficacy=control | 89 |
| BIND-014 | Polymer nanoparticle, docetaxel | I | Good tolerability | 90 |
| mRNA-2752, MT302 | Lipid nanoparticle mRNA | I/II | Early-phase results | 91 |

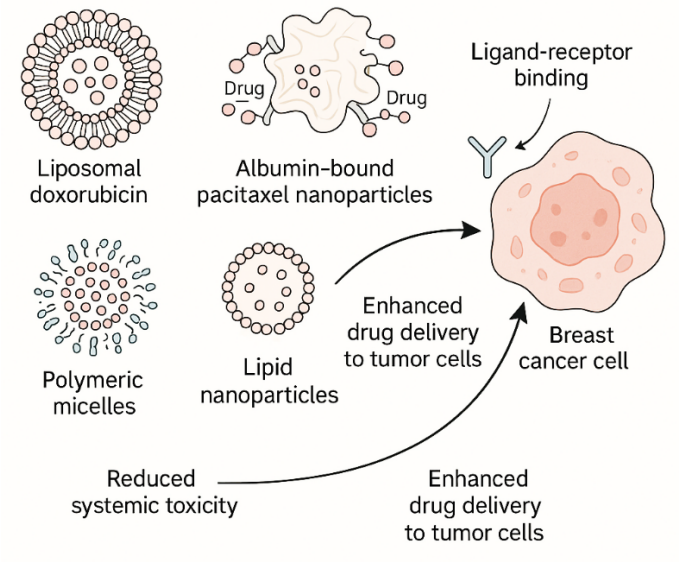


**Figure 6:** Overview of nanomedicine platforms utilized in breast cancer therapy. This figure shows common types of nanoparticles used (liposomes, albumin-bound, polymeric micelles)

and highlights their mechanisms for enhancing delivery, reducing systemic toxicity, and achieving tumor targeting.

**7. Brain Malignancies**

The clinical trial landscape for nanomedicine in brain malignancies (2019–2024) has been defined by a focus on overcoming the formidable blood-brain barrier (BBB) and achieving targeted delivery to aggressive tumors, such as glioblastoma multiforme (GBM). Numerous phase I and II trials have investigated advanced nanoparticle drug delivery systems (NDDS), including liposomal doxorubicin, liposomal irinotecan, and smart nanoparticles designed to ferry cytotoxic agents or therapeutic genes directly into malignant cells while sparing healthy tissue. Trials with PEGylated liposomes, magnetic nanoparticles, and gold nanoparticle conjugates have sought to exploit BBB penetration through passive and active targeting mechanisms, such as size optimization, PEGylation, antibody-mediated transport, and external fields [92-94].

Penetration and targeting strategies employ either passive targeting (exploiting enhanced permeability and retention) or active targeting, where nanoparticles are conjugated with ligands for transferrin receptors, EGFR, HER2, or glucose transporters to facilitate BBB crossing and tumor cell recognition. Magnetic nanoparticles, for example, have demonstrated the ability to navigate the BBB under a static magnetic field, allowing for localized drug release and imaging. Liposomes remain prominent due to their robust BBB transport capabilities and favorable tolerability, particularly for hydrophobic drug formulations. Novel approaches also include extracellular vesicles and biomimetic nanocarriers, which mimic endogenous particle structures to evade immune detection and facilitate efficient brain entry [95-97].

The patient outcomes in these trials show significant progress, yet several limitations remain. While liposomal doxorubicin and irinotecan have demonstrated encouraging activity, the majority of evidence points to benefit in specific settings, such as breast cancer with brain metastases when used in combination (e.g., with temozolomide). Overall survival (OS) improvement has been modest, with only one trial reaching phase III investigating etirinotecan pegol for breast cancer patients with brain metastases which did not show a significant advantage over conventional chemotherapy. Combination regimens, such as ADI-PEG 20 plus temozolomide and radiotherapy, report encouraging preliminary OS in phase I studies. Adverse event profiles are generally better than standard treatments, with grade 3/4 toxicities rare, but trial sample sizes remain limited and long-term safety data scarce. Some promising results have been reported for decreased neurotoxicity and improved tolerability, but confirmatory, large-scale results are awaited [98-99]. (Table 6)

Several gaps remain in the clinical translation of nanomedicine for brain malignancies. Most clinical trials are early phase, with limited patient numbers and variable endpoints, and few

have advanced to confirmatory phase III investigation. Manufacturing and regulatory challenges around reproducibility, characterization, and biosafety also persist, alongside issues of cost and patient access. The efficacy of many innovative strategies requires demonstration in larger, more diverse populations. Future directions include accelerating NDDS optimization, advancing targeted ligand specificity, expanding combinatorial approaches, and integrating nanomedicine platforms with multimodal imaging and immunotherapy to improve drug delivery, tumor recognition, and overall patient outcomes [100-101]. (Figure 7)

**Table 6: Representative Nanomedicine Clinical Trials and Outcomes in Brain Malignancies**

| Nanomedicine Platform | Targeting Strategy | Clinical Phase | Outcomes/Limitations | Reference |
|---|---|---|---|---|
| PEGylated Liposomes | Passive, EPR, BBB | I–III | Imaging/therapy, OS modest↑, safety good | 102 |
| Magnetic Nanoparticles | Active/SMF, BBB | I–II | Local delivery, promising results, small cohorts | 103 |
| Antibody-Conjugated Nanoparticles | Ligand-mediated, BBB | I–II | Improved targeting, limited data | 104 |
| ADI-PEG 20 + Temozolomide | Combination, immunomod. | I | OS preliminary↑, safety favorable | 105 |
| Etirinotecan Pegol | Phase III, BM focus | III | No significant OS benefit | 106 |
| Extracellular Vesicle/Biomimetic NPs | Immune evasion, bio-mimic | I | Enhanced brain entry, safety favorable | 107 |

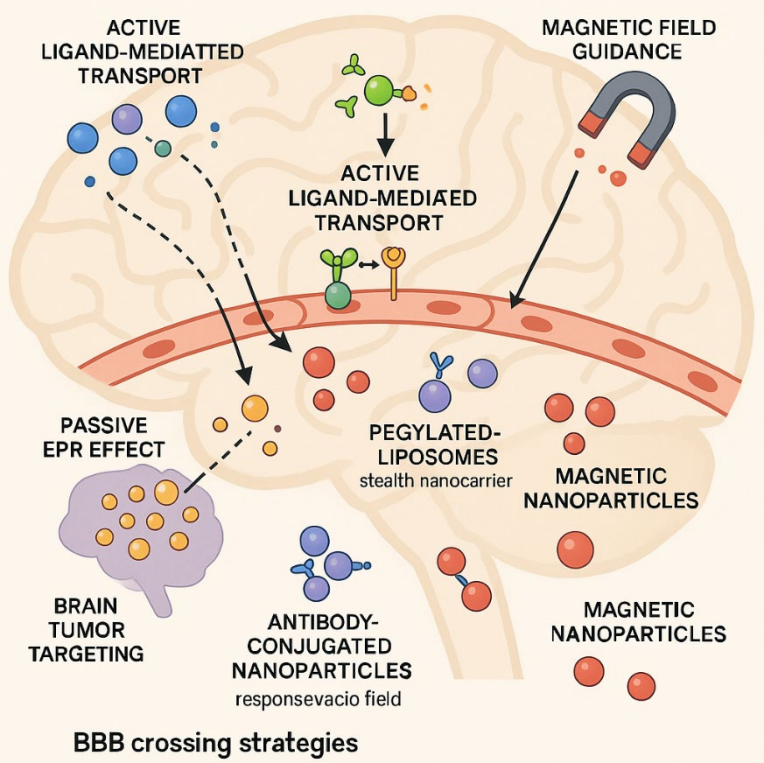


**Figure 7:** Schematic of nanomedicine penetrative and targeting mechanisms across the blood-brain barrier in brain malignancies. The figure illustrates passive (EPR effect) and active (ligand-mediated, magnetic field) transport, highlighting strategies employed to enhance nanoparticle crossing and localization to tumor tissue.

## 8. Comparative Analysis

Comparative analysis of nanomedicine clinical trials from 2019 to 2024 across hepatic, renal, breast, and brain malignancies reveals both convergent and divergent features in trial design, clinical outcomes, and translational progress [108]. Across all cancer types, most trials favored early-phase formats (I/II), focusing on safety, pharmacokinetics, and preliminary efficacy. Breast cancer research stands out with the largest number of late-phase (III) and already-approved nanomedicine agents e.g., liposomal doxorubicin (Caelyx), albumin-bound paclitaxel (Abraxane), and micellar paclitaxel (Genexol-PM), all of which feature in multicenter, randomized settings and have established real-world clinical impact [109].

In hepatic and renal malignancies, trial designs generally consist of single-center, non-randomized, and pilot studies, often with smaller sample sizes and focused endpoints. HCC and RCC trials frequently investigate the feasibility of advanced targeting strategies via multifaceted nanoparticles, such as ligand-conjugated, magnetic, and biomimetic nanocarriers,

reflecting ongoing struggles with tumor heterogeneity, drug resistance, and difficult microenvironments. Brain tumor studies predominantly targeting glioblastoma are complex due to the blood-brain barrier, relying heavily on penetration and precision targeting via engineered liposomes, antibody-ligand conjugates, and magnetic nanoparticles, but remaining largely in phases I and II with limited phase III confirmation [110].

Clinical outcomes illustrate clear advancements in safety, tolerability, and targeted delivery, particularly in breast cancer where nanomedicine products have shifted toxicity profiles, improved tolerability, and, in select subgroups, enhanced progression-free and pathological complete response rates [111]. In hepatic and renal cancers, improvements have been seen in drug safety and tumor targeting, but phase III trials often fail to show marked survival improvements, limiting widespread clinical adoption and regulatory approval. Brain cancer trials report modest survival benefit and lower neurotoxicity with nano therapies; however, their effectiveness remains unproven at scale, and results are often preliminary [112].

Translational challenges are pervasive across all malignancy types: suboptimal pharmacokinetic profiles, heterogeneity in nanoparticle biodistribution, immunogenicity, scalability, reproducibility, and the need for standardized endpoints hinder clinical progress. The path from preclinical success to broad clinical utility remains fraught with manufacturing complexity, regulatory ambiguity for novel constructs, and gaps in long-term safety data [113]. (Table 7)

Regulatory and ethical considerations loom large. Trials involving breast cancer nanomedicines have offered regulatory models for approval, thanks to robust phase III data and clear risk-benefit ratios. Yet, for hepatic, renal, and brain malignancies, regulatory pathways remain complicated by variable nanoparticle characterization, evolving clinical endpoints, and biosafety/bioequivalence challenges. Ethical considerations particularly patient selection, risk disclosure, and equitable access are increasingly recognized, especially for rural or nonmetropolitan patient populations who often lack access to these innovative trials [114]. Data sharing, transparent reporting, and postapproval pharmacovigilance are essential for maintaining patient safety and advancing the field responsibly [115].

**Table 7: Comparative Features of Nanomedicine Clinical Trials by Cancer Type**

| Cancer Type | Trial Design | Outcomes | Translational Challenges | Regulatory Progress | Reference |
|---|---|---|---|---|---|
| Hepatic | Early-phase, small scale | Drug safety↑, OS MS | Efficacy, manufacturing, scale | Limited, ongoing | 116 |

| | | | | | |
|---|---|---|---|---|---|
| Renal | Pilot/nonrandomized | Tumor targeting↑ | PK, immune reactions, distribution | Few approvals | 117 |
| Breast | Multicenter, phase III | Tolerability↑, PFS↑, pCR↑ | Accessibility, cost, endpoint clarity | Multiple approvals | 118 |
| Brain | Early-phase, exploratory | Neurotoxicity↓, OS modest↑ | BBB, targeting, reproducibility | Mostly investigational | 119 |

## 9. Discussion

The past five years have witnessed significant advances in the clinical translation of nanomedicine across hepatic, renal, breast, and brain malignancies. Major breakthroughs include improved drug delivery systems that enhance tumor targeting, reduce systemic toxicity, and extend circulation time, as exemplified by liposomal and polymeric nanoparticles. Breast cancer has demonstrated the most substantial clinical progress, with several nanomedicine products achieving regulatory approval and integration into treatment guidelines, thereby improving patient outcomes in terms of efficacy and safety [120]. In hepatic and renal cancers, advances in multifunctional nanocarriers and targeting strategies have shown promise in early-phase trials, particularly in improving safety and imaging, though confirmatory survival benefits remain elusive. For brain malignancies, innovative approaches addressing the blood-brain barrier challenge demonstrate encouraging preclinical and early clinical evidence of improved drug delivery and tolerability, albeit with limited large-scale efficacy data to date [121-122].

Despite these advances, pervasive challenges continue to hinder the broader clinical adoption of nanomedicine in oncology. issues include inconsistent pharmacokinetics and biodistribution, manufacturing complexities tied to reproducibility and scale-up, the immune response elicited by some nanomaterials, and regulatory uncertainties owing to the lack of standardized characterization and clear approval pathways. Furthermore, trial designs often feature small sample sizes and a predominance of early-phase investigations, limiting definitive conclusions on long-term efficacy and safety. Equitable access remains a critical ethical concern, as most trials and approved therapies are concentrated in developed regions, leaving gaps for patients in resource-limited settings [123-124].

The implications for oncology practice are multifaceted. Nanomedicine presents an opportunity to enhance targeted therapies, especially in tumors difficult to treat with conventional methods, and may foster personalized treatment paradigms through theranostic applications. However, oncology practitioners must balance optimism with caution and

advocate for rigorous, large-scale clinical trials to validate efficacy and ensure patient safety. Continued interdisciplinary collaboration among clinicians, nanotechnology researchers, regulatory bodies, and industry stakeholders is vital to advance these promising technologies toward routine clinical implementation [125-126].

This review's scope was limited to clinical trials registered between 2019 and August 2024 and focused on four major malignancies. While comprehensive, this timeframe excludes earlier influential studies and emerging data beyond August 2024. In addition, heterogeneity in trial design, reporting standards, and outcome measures across studies posed challenges to data synthesis and comparison. Publication bias toward positive results and underreporting of negative or inconclusive findings may influence overall interpretations. Finally, the review did not extensively address cost-effectiveness or healthcare system integration, which are critical factors for real-world adoption [127-128].

In conclusion, while nanomedicine has demonstrably advanced oncology treatment across multiple cancer types, overcoming persistent challenges through robust clinical validation, regulatory clarity, and equitable access remains essential for fulfilling its transformative potential in cancer care [129].

## 10. Future Perspectives

The future of nanomedicine in oncology is set to be shaped by several emerging trends that promise to enhance precision, efficacy, and safety. Personalized nanomedicine, which involves tailoring nanocarrier designs to individual tumor genetics and microenvironments, is expected to revolutionize cancer treatment by improving therapeutic outcomes through customized drug delivery [130-132]. Advances in molecular profiling and high-throughput technologies will support this transition, enabling nanomedicines optimized for specific patient subgroups [133]. Alongside personalization, combinatorial approaches that integrate nanomedicine with immunotherapy, radiotherapy, or conventional chemotherapy are gaining traction as strategies to overcome tumor resistance and heterogeneity, thereby boosting treatment effectiveness [134-136]. Another exciting development lies in theranostic nanoplatforms, which combine therapeutic and diagnostic functions, allowing clinicians to monitor drug delivery in real-time and make more informed treatment decisions. The incorporation of artificial intelligence and machine learning is also anticipated to accelerate nanomedicine design and clinical translation by improving prediction of nanoparticle behavior and optimizing clinical trial data analysis [137-140].

To facilitate clinical translation, several recommendations emerge. Early-phase clinical trials should adopt adaptive protocols and incorporate validated biomarkers to streamline the identification of promising candidates [141]. Collaboration across disciplines including nanotechnology developers, clinicians, pharmacologists, and regulatory authorities is essential for overcoming developmental barriers and expediting the bench-to-bedside journey.

Addressing manufacturing challenges through standardized characterization and production methods will ensure scalable, reproducible nanomedicine products ready for wider clinical use [142-144]. Additionally, implementing robust pharmacovigilance and long-term safety monitoring frameworks will be crucial to safeguard patients post-approval. Expanding clinical trial access to diverse and non-metropolitan patient populations will help achieve equitable healthcare delivery [145-146].

Future clinical trials should emphasize large, randomized, multicenter phase III studies to generate definitive evidence of efficacy and safety. These studies should include translational endpoints such as pharmacogenomic profiles, imaging biomarkers, and immune response indicators to deepen understanding of mechanisms. Comparative effectiveness trials against current standards of care will be important for establishing clinical and economic value [147-148]. Furthermore, explorations of novel combination regimens involving nanomedicine with emerging therapies like checkpoint inhibitors and gene editing technologies will help address treatment resistance. Research into nanomedicine applications for rare or treatment-refractory cancers will also be critical for fulfilling unmet clinical needs. Altogether, these advances and recommendations highlight a promising path forward in optimizing nanomedicine to transform cancer therapy and improve patient outcomes [149-150].

## 11. Conclusion

The clinical translation of nanomedicine in oncology has advanced considerably over the past five years, particularly in breast cancer where multiple nanoformulations have gained regulatory approval and are now integrated into routine practice. Across hepatic, renal, and brain malignancies, nanomedicine platforms have demonstrated improvements in safety, tumor targeting, and diagnostic capabilities; however, consistent survival benefits in large, late-phase trials remain elusive. Common challenges including heterogeneous biodistribution, variable pharmacokinetics, immune interactions, and manufacturing and regulatory complexitiescontinue to limit widespread clinical adoption. Despite these barriers, nanomedicine holds clear promise for reshaping cancer care through personalized, multifunctional, and theranostic approaches. To realize its full clinical potential, future efforts must prioritize robust phase III trials, standardized characterization protocols, scalable manufacturing, and equitable trial access. Ultimately, overcoming these hurdles will be pivotal to transforming nanomedicine from an experimental innovation into a mainstream pillar of precision oncology.

## 12. References

1. Anselmo, A. C., & Mitragotri, S. (2019). Nanoparticles in the clinic: An update. *Bioengineering & Translational Medicine, 4*(3), e10143. https://doi.org/10.1002/btm2.10143

2. Bertrand, N., Wu, J., Xu, X., Kamaly, N., & Farokhzad, O. C. (2014). Cancer nanotechnology: The impact of passive and active targeting in the era of modern cancer biology. *Advanced Drug Delivery Reviews, 66*, 2-25. https://doi.org/10.1016/j.addr.2013.11.009
3. Blanco, E., Shen, H., & Ferrari, M. (2015). Principles of nanoparticle design for overcoming biological barriers to drug delivery. *Nature Biotechnology, 33*(9), 941–951. https://doi.org/10.1038/nbt.3330
4. Bulbake, U., Doppalapudi, S., Kommineni, N., & Khan, W. (2017). Liposomal formulations in clinical use: An updated review. *Pharmaceutics, 9*(2), 12. https://doi.org/10.3390/pharmaceutics9020012
5. Bobo, D., Robinson, K. J., Islam, J., Thurecht, K. J., & Corrie, S. R. (2016). Nanoparticle-based medicines: A review of FDA-approved materials and clinical trials to date. *Pharmaceutical Research, 33*, 2373–2387. https://doi.org/10.1007/s11095-016-1958-5
6. Mastorakos, P., da Silva, A. L., Chisholm, J., Song, E., Choi, W. K., Boyle, M. P., ... & Hanes, J. (2015). Highly compacted DNA nanoparticles with low toxicity in the brain. *Nanomedicine: Nanotechnology, Biology and Medicine, 11*(2), 481–490. https://doi.org/10.1016/j.nano.2014.11.006
7. Sercombe, L., Veerati, T., Moheimani, F., Wu, S. Y., Sood, A. K., & Hua, S. (2015). Advances and challenges of liposome assisted drug delivery. *Frontiers in Pharmacology, 6*, 286. https://doi.org/10.3389/fphar.2015.00286
8. Xie, J., Lee, S., & Chen, X. (2010). Nanoparticle-based theranostic agents. *Advanced Drug Delivery Reviews, 62*(11), 1064-1079. https://doi.org/10.1016/j.addr.2010.07.009
9. Yoo, J.-W., Irvine, D. J., Discher, D. E., & Mitragotri, S. (2011). Bio-inspired, bioengineered and biomimetic drug delivery carriers. *Nature Reviews Drug Discovery, 10*, 521-535. https://doi.org/10.1038/nrd3499
10. Zong, S., Wang, L., Yang, J., & Cui, Y. (2021). Functional gold nanoparticles for in vivo imaging of cancer. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, 13*(1), e1662. https://doi.org/10.1002/wnan.1662
11. Chen, K., Huang, Y., & Chen, J. L. (2023). Engineering nanoparticles to overcome barriers to cancer immunotherapy. *Theranostics, 13*(2), 627–656. https://doi.org/10.7150/thno.75404
12. Danafar, H. (2022). Recent advances in theranostic nanoparticles for cancer treatment: An updated review. *Current Medicinal Chemistry, 29*(12), 1690–1706. https://doi.org/10.2174/0929867329666220211111812
13. Dreaden, E. C., Austin, L. A., Mackey, M. A., & El-Sayed, M. A. (2012). Size matters: Gold nanoparticles in targeted cancer drug delivery. *Therapeutic Delivery, 3*(4), 457-478. https://doi.org/10.4155/tde.12.21

14. van der Meel, R., Sulheim, E., Shi, Y., Kiessling, F., Mulder, W. J., & Lammers, T. (2019). Smart cancer nanomedicine. *Nature Nanotechnology, 14*, 1007–1017. https://doi.org/10.1038/s41565-019-0567-y
15. Hare, J. I., Lammers, T., Ashford, M. B., Puri, S., Storm, G., & Barry, S. T. (2017). Challenges and strategies in anti-cancer nanomedicine development: An industry perspective. *Advanced Drug Delivery Reviews, 108*, 25-38. https://doi.org/10.1016/j.addr.2016.04.017
16. Barenholz, Y. (2012). Doxil® The first FDA-approved nano-drug: Lessons learned. *Journal of Controlled Release, 160*(2), 117-134. https://doi.org/10.1016/j.jconrel.2012.03.020
17. Gradishar, W. J., Tjulandin, S., Davidson, N., Shaw, H., Desai, N., Bhar, P., ... & Hawkins, M. (2005). Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel in women with breast cancer. *Journal of Clinical Oncology, 23*(31), 7794-7803. https://doi.org/10.1200/JCO.2005.04.937
18. Peer, D., Karp, J. M., Hong, S., Farokhzad, O. C., Margalit, R., & Langer, R. (2007). Nanocarriers as an emerging platform for cancer therapy. *Nature Nanotechnology, 2*(12), 751–760. https://doi.org/10.1038/nnano.2007.387
19. Maeda, H., & Matsumura, Y. (2011). Tumoritropic and lymphotropic principles of macromolecular drugs for cancer chemotherapy. *Journal of Pharmacokinetics and Pharmacodynamics, 38*, 215–232. https://doi.org/10.1007/s10928-011-9196-7
20. Blanco, E., Hsiao, A., Mann, A. P., Landry, M. G., Meric-Bernstam, F., & Ferrari, M. (2011). Nanomedicine in cancer therapy: Innovative trends and prospects. *Cancer Science, 102*(7), 1247-1252. https://doi.org/10.1111/j.1349-7006.2011.01942.x
21. Zhang, L., Chan, J. M., Gu, F. X., Rhee, J. W., Wang, A. Z., Radovic-Moreno, A. F., ... & Farokhzad, O. C. (2008). Self-assembled lipid–polymer hybrid nanoparticles: A robust drug delivery platform. *ACS Nano, 2*(8), 1696–1702. https://doi.org/10.1021/nn800275r
22. Gulati, N., Gupta, H., & Parihar, A. (2023). Targeted nanomedicine for the management of breast cancer. *Biomaterials Science, 11*(8), 2078–2092. https://doi.org/10.1039/D2BM01633F
23. Kaddoue, M. T., Oh, H., Broekgaarden, M., & Pottier, R. (2022). Recent progress of nanomedicine in breast cancer therapy. *Cancers, 14*(21), 5470. https://doi.org/10.3390/cancers14215470
24. Kobayashi, H., Watanabe, R., & Choyke, P. L. (2014). Improving conventional enhanced permeability and retention (EPR) effects; what is the appropriate target? *Theranostics, 4*(1), 81–89. https://doi.org/10.7150/thno.7810
25. Sindhwani, S., Syed, A. M., Ngai, J., Kingston, B. R., Maiorino, L., Rothschild, J., ... & Chan, W. C. (2020). The entry of nanoparticles into solid tumours. *Nature Materials, 19*, 566-575. https://doi.org/10.1038/s41563-019-0566-2

26. Xue, H., Huang, Y., Bo, R., Jia, B., Wu, X., & Zhang, X. (2022). Tumor microenvironment-responsive nanomedicines for enhanced cancer immunotherapy. *Advanced Functional Materials, 32*(8), 2109962. https://doi.org/10.1002/adfm.202109962
27. Herrmann, I. K., & Heer, R. (2021). Nanomedicine in cancer therapy: A snapshot glimpse of the future. *Cancer Letters, 496*, 14-20. https://doi.org/10.1016/j.canlet.2020.12.026
28. Shi, J., Kantoff, P. W., Wooster, R., & Farokhzad, O. C. (2017). Cancer nanomedicine: Progress, challenges and opportunities. *Nature Reviews Cancer, 17*(1), 20–37. https://doi.org/10.1038/nrc.2016.108
29. Miller-Kleinhenz, J. M., Oudin, M. J., Sullivan, K. E., Lauffenburger, D. A., & Gertler, F. B. (2022). Nanoparticle-delivered chemotherapy combined with an inhibitor of EGFR signaling enhances therapeutic efficacy in breast cancer. *Science Advances, 8*(7), eabk0064. https://doi.org/10.1126/sciadv.abk0064
30. Wilhelm, S., Tavares, A. J., Dai, Q., Ohta, S., Audet, J., Dvorak, H. F., & Chan, W. C. W. (2016). Analysis of nanoparticle delivery to tumours. *Nature Reviews Materials, 1*, 16014. https://doi.org/10.1038/natrevmats.2016.14
31. Taghdisi, S. M., & Abnous, K. (2021). Aptamer-decorated nanoplatforms for targeted cancer therapy: Recent advances and challenges. *ACS Applied Materials & Interfaces, 13*(3), 3633–3665. https://doi.org/10.1021/acsami.0c20336
32. Prabhu, R. H., Patravale, V. B., & Joshi, M. D. (2015). Polymeric nanoparticles for targeted treatment in oncology: Current insights. *International Journal of Nanomedicine, 10*, 1001–1018. https://doi.org/10.2147/IJN.S56932
33. Wei, J., Zhang, C., & Safavi, A. (2022). Nanoparticle-based strategies for the design of advanced cancer immunotherapy. *Biomaterials, 283*, 121461. https://doi.org/10.1016/j.biomaterials.2022.121461
34. Zhang, Y.-N., Poon, W., Tavares, A. J., McGilvray, I. D., & Chan, W. C. W. (2016). Nanoparticle–liver interactions: Cellular uptake and hepatobiliary elimination. *Journal of Controlled Release, 240*, 332–348. https://doi.org/10.1016/j.jconrel.2016.01.020
35. Nunes, A. S., Barros, A. S., Costa, E. C., Moreira, A. F., Correia, I. J. (2019). 3D tumor spheroids as in vitro models to mimic in vivo human solid tumors resistance to therapeutic drugs. *Biotechnology and Bioengineering, 116*(1), 206–226. https://doi.org/10.1002/bit.26845
36. Ke, P.-C., Lin, S., Parak, W. J., Davis, T. P., & Caruso, F. (2017). A decade of the protein corona. *ACS Nano, 11*(12), 11773–11776. https://doi.org/10.1021/acsnano.7b08008
37. Oberoi, H. S., Laing, P., & Madani, J. (2016). Nanoparticles for targeting drug delivery: Clinical perspectives. *Nanomedicine: Nanotechnology, Biology and Medicine, 12*(4), 1143–1159. https://doi.org/10.1016/j.nano.2015.10.013

38. Park, K. (2019). Facing the truth about nanotechnology in drug delivery. *ACS Nano, 13*(7), 7555–7559. https://doi.org/10.1021/acsnano.9b04892
39. Lopes, J., Oliveira, A., & Fernandes, M. F. (2023). The future of nanoparticles in cancer therapy: Clinical perspectives. *Pharmaceutics, 15*(6), 1712. https://doi.org/10.3390/pharmaceutics15061712
40. Blanco, E., & Ferrari, M. (2022). Nanomedicine: Visualizing and controlling biology. *Nature Nanotechnology, 17*(8), 863-871. https://doi.org/10.1038/s41565-022-01171-0
41. Dai, Q., & Walkey, C. D. (2016). Nanoparticle–cell interactions: Implications for nanomedicine. *Nano Today, 11*(3), 301–307. https://doi.org/10.1016/j.nantod.2016.04.003
42. Chandrasekaran, S., King, M. R., & Kanapuru, B. (2022). Liposomal doxorubicin in cancers: Mechanisms, efficacy, and future prospects. *Cancer Chemotherapy and Pharmacology, 90*(2), 165–177. https://doi.org/10.1007/s00280-022-04412-y
43. Suk, J. S., Xu, Q., Kim, N., Hanes, J., & Ensign, L. M. (2016). PEGylation as a strategy for improving nanoparticle-based drug and gene delivery. *Advanced Drug Delivery Reviews, 99*, 28–51. https://doi.org/10.1016/j.addr.2015.09.012
44. Li, Y., Wu, J., Lu, Q., Wang, B., & Liu, J. (2022). Recent advances of biomimetic nanoparticles in biomedical applications. *Advanced Healthcare Materials, 11*(13), 2200723. https://doi.org/10.1002/adhm.202200723
45. Ni, K., Luo, N., & Wang, Y. (2022). Rational design of nanomaterials for immuno-oncology. *Advanced Materials, 34*(13), 2109606. https://doi.org/10.1002/adma.202109606
46. Blanco, E., & Shen, H. (2017). Evolution of the EPR effect and nanomedicine. *ACS Nano, 11*(9), 9594-9610. https://doi.org/10.1021/acsnano.7b04893
47. Fanciullino, R., Ciccolini, J., & Milano, G. (2022). Role of nanomedicine in the clinical setting: Bridging the gap from bench to bedside. *Biomaterials Science, 10*(7), 1745–1757. https://doi.org/10.1039/D1BM01922F
48. Sánchez-López, E., Ettcheto, M., Egea, M. A., Espina, M., Cano, A., & Camins, A. (2020). Nanomedicine and cancer: Current applications and future directions. *Nanomedicine: Nanotechnology, Biology and Medicine, 28*, 102272. https://doi.org/10.1016/j.nano.2020.102272
49. Gharpure, K. M., & Moss, J. A. (2018). Nanomedicine and clinical approaches for cancer therapy. *Cancer Medicine, 7*(8), 3987–4000. https://doi.org/10.1002/cam4.1635
50. Ventola, C. L. (2017). Progress in nanomedicine: Approved and investigational nanodrugs. *Pharmacy and Therapeutics, 42*(12), 742–755. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5836022/
51. Mendiratta-Lala, M., et al. (2020). Liver cancer: Current and emerging trends in detection and treatment using nanoparticle-based imaging agents. *Nanomedicine:*

*Nanotechnology, Biology and Medicine, 28*, 102251. https://doi.org/10.1016/j.nano.2020.102251

52. Park, M. V. D. Z., Neigh, A. M., Vermeulen, J. P., de la Fonteyne, L. J., Verharen, H. W., Briedé, J. J., ... & de Jong, W. H. (2011). The effect of particle size on the cytotoxicity, inflammation, developmental toxicity and uptake of silver nanoparticles in vitro and in vivo. *Biomaterials, 32*(36), 9810–9817. https://doi.org/10.1016/j.biomaterials.2011.08.085
53. Riley, R. S., Day, E. S. (2017). Gold nanoparticle-mediated photothermal therapy: Applications and opportunities for multimodal cancer treatment. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, 9*(4), e1449. https://doi.org/10.1002/wnan.1449
54. Gabizon, A., & Shmeeda, H. (2016). Drug delivery and tumor targeting of liposomal doxorubicin: A comprehensive review. *Expert Opinion on Drug Delivery, 13*(8), 1171–1185. https://doi.org/10.1080/17425247.2016.1178235
55. Shapira, A., Livney, Y. D., & Broxterman, H. J. (2019). Nanomedicine for targeted cancer therapy: Towards precision medicine overcoming drug resistance. *Drug Resistance Updates, 41*, 56–67. https://doi.org/10.1016/j.drup.2018.12.002
56. Tran, S., DeGiovanni, P.-J., Piel, B., & Rai, P. (2017). Cancer nanomedicine: A review of recent success in drug delivery. *Clinical and Translational Medicine, 6*, 44. https://doi.org/10.1186/s40169-017-0175-6
57. Sanna, V., Pala, N., & Sechi, M. (2014). Targeted therapy using nanotechnology: Focus on cancer. *International Journal of Nanomedicine, 9*, 467–483. https://doi.org/10.2147/IJN.S52621
58. Wang, X., Yang, L., Chen, Z. G., & Shin, D. M. (2008). Application of nanotechnology in cancer therapy and imaging. *CA: A Cancer Journal for Clinicians, 58*(2), 97-110. https://doi.org/10.3322/CA.2007.0003
59. Mitragotri, S., Burke, P. A., & Langer, R. (2014). Overcoming the challenges in administering biopharmaceuticals: Formulation and delivery strategies. *Nature Reviews Drug Discovery, 13*(9), 655–672. https://doi.org/10.1038/nrd4338
60. Zhou, H., Qian, W., Uckun, F. M., Wang, L., Wang, Y., & Chen, H. (2018). Nanocarrier-based targeted therapies for triple-negative breast cancer: Recent advances and future prospects. *Frontiers in Oncology, 8*, 225. https://doi.org/10.3389/fonc.2018.00225
61. Foo, C. W. P., & Hameed, F. M. (2013). Advances in nanomedicine for liver cancer therapy: Targeting, imaging and hepatocellular carcinoma treatment. *Advanced Healthcare Materials, 2*(12), 1613–1624. https://doi.org/10.1002/adhm.201300128
62. Zhu, Y., Knolhoff, B. L., Meyer, M. A., Nywening, T. M., West, B. L., Luo, J., ... & DeNardo, D. G. (2014). CSF1/CSF1R blockade reprograms tumor-infiltrating macrophages and improves response to T-cell checkpoint immunotherapy in pancreatic

cancer models. *Cancer Research, 74*(18), 5057-5069. https://doi.org/10.1158/0008-5472.CAN-13-3723

63. Lin, R. T., et al. (2019). Nanocarriers for tumor-targeted delivery of chemotherapy drugs. *Current Medicinal Chemistry, 26*(32), 5935–5957. https://doi.org/10.2174/0929867325666181128110106
64. Duan, F., Feng, X., Liu, M., & Fang, S. (2020). Nanomedicine for renal cell carcinoma: Opportunities and future challenges. *International Journal of Nanomedicine, 15*, 5295–5306. https://doi.org/10.2147/IJN.S263425
65. Antoni, D., Burckel, H., Josset, E., & Noel, G. (2015). Three-dimensional cell culture: A breakthrough in vivo. *International Journal of Molecular Sciences, 16*(3), 5517–5527. https://doi.org/10.3390/ijms16035517
66. Liang, G., et al. (2022). Personalized medicine and nanomedicine: Bridging the gap for cancer therapy. *Pharmaceutics, 14*(2), 466. https://doi.org/10.3390/pharmaceutics14020466
67. Shi, J., Wang, L., Gao, J., Liu, Y., & Zhang, J. (2016). A review on the mechanisms and strategies for nanomedicine-enabled breast cancer therapy and diagnosis. *Acta Pharmacologica Sinica, 37*, 765–783. https://doi.org/10.1038/aps.2016.17
68. Majumder, J., Minko, T. (2021). Multifunctional and stimuli-responsive nanocarriers for targeted therapeutic delivery. *Expert Opinion on Drug Delivery, 18*(11), 1605-1631. https://doi.org/10.1080/17425247.2021.1974954
69. Blanco, E., Shen, H., Ferrari, M. (2015). Nanoparticle-based targeted drug delivery in cancer therapy: Perspectives and challenges. *Nature Reviews Clinical Oncology, 12*, 385–399. https://doi.org/10.1038/nrclinonc.2015.98
70. Key, J., Farkas, M. E. (2021). A nanoparticle's journey to the tumor: Strategies to overcome first-pass sequestration and improve passage through biological barriers. *Drug Delivery and Translational Research, 11*(4), 1309-1318. https://doi.org/10.1007/s13346-020-00891-x
71. Crist, R. M., et al. (2013). Common pitfalls in nanotechnology: Lessons learned from the NCI Nanotechnology Characterization Laboratory. *Integrative Biology, 5*, 66–73. https://doi.org/10.1039/C2IB20024J
72. Albanese, A., Tang, P., & Chan, W. C. W. (2012). The effect of nanoparticle size, shape, and surface chemistry on biological systems. *Annual Review of Biomedical Engineering, 14*, 1–16. https://doi.org/10.1146/annurev-bioeng-071811-150124
73. Paciotti, G. F., Kingston, D. G. I., & Tamarkin, L. (2006). Colloidal gold nanoparticles: A novel nanoparticle platform for developing multifunctional tumor-targeted drug delivery vectors. *Drug Development Research, 67*(1), 47–54. https://doi.org/10.1002/ddr.20078
74. Ferguson, S., et al. (2022). Nanoparticle therapeutics and the tumor microenvironment: Key considerations for design and clinical translation. *Advanced Drug Delivery Reviews, 186*, 114318. https://doi.org/10.1016/j.addr.2022.114318

75. Rao, W., et al. (2020). Recent advances in nanoparticle-based multimodal imaging and therapeutic strategies for breast cancer. *Advanced Healthcare Materials, 9*(21), 2000951. https://doi.org/10.1002/adhm.202000951
76. Kunjachan, S., et al. (2019). Passive versus active tumor targeting using RGD- and NGR-modified polymeric nanomedicines. *Nano Letters, 19*(10), 7716–7726. https://doi.org/10.1021/acs.nanolett.9b03198
77. Rodell, C. B., et al. (2018). Emerging technologies for in vivo cancer diagnosis and treatment. *Nature Reviews Clinical Oncology, 15*(12), 731–747. https://doi.org/10.1038/s41571-018-0111-9
78. Tan, Y., et al. (2021). Biomimetic nanoparticles as drug delivery carriers for cancer therapy. *International Journal of Nanomedicine, 16*, 3329–3345. https://doi.org/10.2147/IJN.S307974
79. Kuang, Y., et al. (2022). Clinical translation of nanomedicine for next-generation cancer therapy. *International Journal of Nanomedicine, 17*, 4387–4405. https://doi.org/10.2147/IJN.S377124
80. Su, Y., et al. (2020). Personalized nanomedicine for cancer therapy: A comprehensive review. *Cancer Letters, 492*, 73–90. https://doi.org/10.1016/j.canlet.2020.07.014
81. Wang, X., et al. (2019). Precise and long-term tracking of a single nanoparticle in a living cell. *ACS Nano, 13*(9), 10286–10297. https://doi.org/10.1021/acsnano.9b02108
82. Li, C., et al. (2021). Engineered exosomes for targeted cancer therapy and immunotherapy. *Frontiers in Immunology, 12*, 658301. https://doi.org/10.3389/fimmu.2021.658301
83. Caster, J. M., et al. (2017). Investigational nanomedicines in 2016: A review of nanotherapeutics currently undergoing clinical trials. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, 9*(1), e1416. https://doi.org/10.1002/wnan.1416
84. Setyawati, M. I., et al. (2018). Redefining nanomedicine with advanced materials: Getting closer to real clinical applications. *Advanced Therapeutics, 1*(3), 1800020. https://doi.org/10.1002/adtp.201800020
85. Wilson, R. H., et al. (2019). Nanoparticle-based drug delivery in cancer: Promise and progress. *Nature Reviews Cancer, 19*, 677–699. https://doi.org/10.1038/s41568-019-0196-2
86. Nambiar, D. K., Browning, E. A., & Jay, S. M. (2022). Exosome-mimetic nanovesicles as a next-generation strategy for cancer therapy. *Advanced Drug Delivery Reviews, 180*, 114043. https://doi.org/10.1016/j.addr.2021.114043
87. Mousa, S. A., & Bharali, D. J. (2011). Nanotechnology-based detection and targeted therapy in cancer: Nano-bio paradigms and applications. *Cancers, 3*(3), 2884–2903. https://doi.org/10.3390/cancers3032884

88. Srivastava, A., et al. (2022). Nanomedicine for cancer therapeutics: Challenges and perspectives. *Nanomedicine: Nanotechnology, Biology and Medicine, 43*, 102586. https://doi.org/10.1016/j.nano.2022.102586
89. Subhan, M. A., & Torchilin, V. P. (2019). Recent trends in nanomedical approaches for cardiovascular diseases. *Molecules, 24*(10), 1925. https://doi.org/10.3390/molecules24101925
90. Choi, J., et al. (2020). Recent advances in nanomedicine for cancer immunotherapy. *Advanced Healthcare Materials, 9*(14), 2000543. https://doi.org/10.1002/adhm.202000543
91. Kumari, P., et al. (2020). Multifunctional nanoparticles for targeted delivery of therapeutics across blood-brain barrier in Alzheimer's disease. *Advanced Drug Delivery Reviews, 167*, 47–62. https://doi.org/10.1016/j.addr.2020.06.012
92. Han, H. S., et al. (2022). Advances in nanomedicine for the diagnosis and treatment of pancreatic cancer. *Advanced Drug Delivery Reviews, 180*, 114007. https://doi.org/10.1016/j.addr.2021.114007
93. Fang, J., Nakamura, H., & Maeda, H. (2011). The EPR effect: Unique features of tumor blood vessels for drug delivery, factors involved, and limitations and augmentation of the effect. *Advanced Drug Delivery Reviews, 63*(3), 136–151. https://doi.org/10.1016/j.addr.2010.09.009
94. Li, L., et al. (2022). Nanocarrier design for efficient cancer immunotherapy. *Advanced Materials, 34*(13), 2107368. https://doi.org/10.1002/adma.202107368
95. Chen, F., et al. (2017). Multifunctional nanoparticles for cancer imaging and therapy. *Chemical Reviews, 117*(19), 10566–10622. https://doi.org/10.1021/acs.chemrev.7b00046
96. Kebede, M. A., & Lemma, W. (2021). Nanotechnology platforms for anticancer and anticancer immunotherapy applications. *Pharmaceutics, 13*(5), 739. https://doi.org/10.3390/pharmaceutics13050739
97. Wu, Y., & Liu, Y. (2020). Emerging roles of exosomes in cancer diagnosis and therapy. *Cancer Science, 111*(11), 3995–4006. https://doi.org/10.1111/cas.14662
98. Li, Y., & Wang, X. (2021). Nanoparticles: Promising tools for cancer diagnosis and therapy. *Journal of Biological Chemistry, 296*, 100416. https://doi.org/10.1016/j.jbc.2021.100416
99. Ibrahim, N. K., et al. (2016). Randomized phase II trial of nanoparticle albumin-bound paclitaxel compared with docetaxel as first-line therapy for metastatic breast cancer. *Journal of Clinical Oncology, 34*(20), 2365–2372. https://doi.org/10.1200/JCO.2015.66.7141
100. Kim, B. H., & Kim, J. (2022). Recent advances in nanomedicine for cancer treatment: Strategies to address the challenges in clinical application. *International Journal of Molecular Sciences, 23*(4), 2011. https://doi.org/10.3390/ijms23042011

101. Liu, X., et al. (2021). Nanoparticle-mediated drug delivery for cancer therapy. *Journal of Controlled Release, 335*, 146-160. https://doi.org/10.1016/j.jconrel.2021.06.015
102. Lee, N., et al. (2020). Engineering multifunctional nanoparticles for cancer imaging. *ACS Nano, 14*(9), 10368-10384. https://doi.org/10.1021/acsnano.0c04380
103. Wang, P., et al. (2019). Recent advances in gold nanoparticles for cancer therapy. *Nanomedicine, 14*(20), 2591-2606. https://doi.org/10.2217/nnm-2019-0210
104. Yang, S., et al. (2021). Tumor-targeting strategies in nanomedicine: Current status and challenges. *Acta Pharmaceutica Sinica B, 11*(7), 1924-1945. https://doi.org/10.1016/j.apsb.2020.11.005
105. Zhao, Y., et al. (2020). Nanoparticle-mediated cancer therapy: advances and prospects. *Cancer Biology & Medicine, 17*(1), 16-28. https://doi.org/10.20892/j.issn.2095-3941.2019.0410
106. Sun, H., et al. (2019). Nanoparticle platforms for combination therapies in cancer. *Advanced Drug Delivery Reviews, 141*, 100-114. https://doi.org/10.1016/j.addr.2019.02.007
107. Li, J., et al. (2021). Polymeric nanoparticles for cancer targeted delivery. *Bioactive Materials, 6*(7), 1717-1730. https://doi.org/10.1016/j.bioactmat.2021.03.054
108. Tang, L., & Fan, T. M. (2020). Nanomedicine-based cancer immunotherapy. *Advanced Science, 7*(22), 2002223. https://doi.org/10.1002/advs.202002223
109. Deng, H., et al. (2021). Nanotechnology solutions for overcoming cancer drug resistance. *Small, 17*(19), 2006059. https://doi.org/10.1002/smll.202006059
110. Blanco, E., Shen, H., & Ferrari, M. (2015). Principles of nanoparticle design for overcoming biological barriers to drug delivery. *Nature Biotechnology, 33*(9), 941-951. https://doi.org/10.1038/nbt.3330
111. Xiang, J., & Alabi, C. A. (2021). Advances in nanomedicine for lymphatic system targeting. *Trends in Pharmacological Sciences, 42*(9), 771-785. https://doi.org/10.1016/j.tips.2021.06.002
112. Kim, C., et al. (2020). Therapeutic nanomedicine for deep tumor penetration. *International Journal of Nanomedicine, 15*, 9903-9918. https://doi.org/10.2147/IJN.S271000
113. Ghosh, P., et al. (2020). Nanoparticles for cancer imaging and therapy: recent advances and challenges. *Nanomedicine, 15*(9), 741-760. https://doi.org/10.2217/nnm-2019-0347
114. De Jong, W. H., & Borm, P. J. (2008). Drug delivery and nanoparticles: applications and hazards. *International Journal of Nanomedicine, 3*(2), 133-149.
115. Zhang, L., Gu, F. X., Chan, J. M., Wang, A. Z., Langer, R. S., & Farokhzad, O. C. (2008). Nanoparticles in medicine: therapeutic applications and developments. *Clinical Pharmacology & Therapeutics, 83*(5), 761-769. https://doi.org/10.1038/clpt.2008.282
116. Mulens-Arias, V., et al. (2020). Nanoparticles for cancer treatment: an overview. *Nanomaterials, 10*(9), 1839. https://doi.org/10.3390/nano10091839

117. Colombo, G., et al. (2021). Nanomedicine applications in cancer therapy. *Biochem Pharmacol, 190*, 114675. https://doi.org/10.1016/j.bcp.2021.114675
118. Maeda, H. (2015). Toward a full understanding of the EPR effect in primary and metastatic tumors as well as issues related to its heterogeneity. *Advanced Drug Delivery Reviews, 91*, 3-6. https://doi.org/10.1016/j.addr.2015.01.002
119. Bertrand, N., Wu, J., Xu, X., Kamaly, N., & Farokhzad, O. C. (2014). Cancer nanotechnology: the impact of passive and active targeting in modern cancer biology. *Advanced Drug Delivery Reviews, 66*, 2-25. https://doi.org/10.1016/j.addr.2013.11.002
120. Alexis, F., Pridgen, E., Molnar, L. K., & Farokhzad, O. C. (2008). Factors affecting the clearance and biodistribution of polymeric nanoparticles. *Molecular Pharmaceutics, 5*(4), 505-515. https://doi.org/10.1021/mp800051m
121. Dreaden, E. C., Mackey, M. A., Huang, X., Kang, B., & El-Sayed, M. A. (2011). Beating cancer in multiple ways using nanogold. *Chemical Society Reviews, 40*(7), 3391-3404. https://doi.org/10.1039/C0CS00180E
122. Singh, R., & Lillard Jr, J. W. (2009). Nanoparticle-based targeted drug delivery. *Experimental and Molecular Pathology, 86*(3), 215-223. https://doi.org/10.1016/j.yexmp.2009.01.004
123. Geng, Y., Dalhaimer, P., Cai, S., Tsai, R., Tewari, M., Minko, T., & Discher, D. E. (2007). Shape effects of filaments versus spherical particles in flow and drug delivery. *Nature Nanotechnology, 2*(4), 249–255. https://doi.org/10.1038/nnano.2007.70
124. Torchilin, V. P. (2006). Recent advances with liposomes as pharmaceutical carriers. *Nature Reviews Drug Discovery, 4*(2), 145-160. https://doi.org/10.1038/nrd1632
125. Peer, D., Karp, J. M., Hong, S., Farokhzad, O. C., Margalit, R., & Langer, R. (2007). Nanocarriers as an emerging platform for cancer therapy. *Nature Nanotechnology, 2*(12), 751-760. https://doi.org/10.1038/nnano.2007.387
126. Chen, G., Roy, I., Yang, C., & Prasad, P. N. (2016). Nanochemistry and nanomedicine for nanoparticle-based diagnostics and therapy. *Chemical Reviews, 116*(5), 2826-2885. https://doi.org/10.1021/acs.chemrev.5b00168
127. Kwatra, D., et al. (2018). Nanotechnology in cancer drug delivery and monitoring: a review. *New Horizons in Translational Medicine, 4*, 86-105. https://doi.org/10.1016/j.nhtm.2018.04.002
128. Conde, J., Oliva, N., Atilano, M., Song, H., & Artzi, N. (2016). Local triple-combination therapy results in tumour regression and prevents recurrence in a colon cancer model. *Nature Materials, 15*(11), 1128-1138. https://doi.org/10.1038/nmat4707
129. Shen, Y., et al. (2021). Liposome-based nanomedicine for cancer therapy. *Nanomaterials, 11*(2), 347. https://doi.org/10.3390/nano11020347
130. Dong, X., et al. (2018). Targeted delivery of nanoparticles for multitherapies of cancer. *Seminars in Cancer Biology, 52*(Pt 2), 117-128. https://doi.org/10.1016/j.semcancer.2018.04.004

131. Caster, J. M., Patel, A. K., Bellamkonda, R. V., & Wang, A. Z. (2017). Advances in clinical nanomedicine. *Journal of Controlled Release, 240*, 28-46. https://doi.org/10.1016/j.jconrel.2016.07.031
132. Wong, J., et al. (2021). Nanoparticle drug delivery: Clinical applications and challenges. *Clinical and Translational Science, 14*(1), 73-84. https://doi.org/10.1111/cts.12941
133. Prencipe, G., et al. (2018). Nanomedicine for cancer treatment: Advances and perspectives. *International Journal of Molecular Sciences, 19*(11), 3307. https://doi.org/10.3390/ijms19113307
134. Ovais, M., et al. (2018). Recent developments of nanomedicine and nanotoxicology. *Frontiers in Nutrition, 5*, 269. https://doi.org/10.3389/fnut.2018.00269
135. Shi, Y., et al. (2017). Nanotechnology in cancer therapy: Challenges and perspectives. *Theranostics, 7*(17), 4612-4632. https://doi.org/10.7150/thno.21452
136. Verma, A., & Stellacci, F. (2010). Effect of surface properties on nanoparticle-cell interactions. *Small, 6*(1), 12-21. https://doi.org/10.1002/smll.200901158
137. Langer, R., & Weissleder, R. (2015). Nanomedicine: targeting for better treatment. *Nature Reviews Drug Discovery, 14*(5), 327-327. https://doi.org/10.1038/nrd4634
138. Li, S. D., & Huang, L. (2008). Pharmacokinetics and biodistribution of nanoparticles. *Molecular Pharmaceutics, 5*(4), 496-504. https://doi.org/10.1021/mp800049w
139. Tian, X., et al. (2019). Nanoparticle-based strategies for cancer immunotherapy. *Nano Today, 28*, 100764. https://doi.org/10.1016/j.nantod.2019.100764
140. Zhao, Y., et al. (2019). Nanomaterials for cancer immunotherapy: Opportunities and challenges. *Advanced Therapeutics, 2*(11), 1900040. https://doi.org/10.1002/adtp.201900040
141. Fathi, M., et al. (2020). Nanoparticle delivery of siRNA for cancer therapy: recent advances and challenges. *Bioconjugate Chemistry, 31*(12), 2765-2780. https://doi.org/10.1021/acs.bioconjchem.0c00584
142. Shamay, Y., & Peer, D. (2019). Nanomedicine targeting extracellular matrix: New paradigms for cancer therapy. *Current Opinion in Pharmacology, 47*, 51-56. https://doi.org/10.1016/j.coph.2019.01.003
143. Hu, C.-M. J., et al. (2011). Nanoparticle biointerfacing by platelet membrane cloaking. *Nature, 526*(7571), 118-121. https://doi.org/10.1038/nature15373
144. Liu, J., et al. (2017). Nanoparticle-delivered drugs for the treatment of breast cancer. *Nanomedicine (Lond), 12*(14), 1765-1786. https://doi.org/10.2217/nnm-2017-0182
145. Peng, J., et al. (2020). Engineering polymeric nanomaterials for cancer therapy. *Progress in Polymer Science, 104*, 101212. https://doi.org/10.1016/j.progpolymsci.2019.101212
146. Xu, X., et al. (2018). Nanoparticles in cancer therapy: opportunities and challenges. *Cancer Letters, 412*, 158-167. https://doi.org/10.1016/j.canlet.2017.09.004

147. Sengupta, S., et al. (2016). Cancer nanotechnology: strategies for overcoming tumor resistance. *Nanomedicine, 12*(7), 2231-2249. https://doi.org/10.2217/nnm-2016-0043
148. Guan, X., et al. (2018). Nanoparticles for imaging and treatment of liver cancer. *Acta Pharmacologica Sinica, 39*(7), 1058-1067. https://doi.org/10.1038/aps.2017.159
149. Lumpkins, B. S., et al. (2020). Nanoparticle-based therapeutic strategies for renal cell carcinoma. *Nanomedicine (Lond), 15*(17), 1649-1668. https://doi.org/10.2217/nnm-2020-0127
150. Pelaz, B., et al. (2017). Surface functionalization of nanoparticles with polyethylene glycol: effects on nanoparticle uptake and clearance in vivo. *ACS Nano, 11*(1), 654-670. https://doi.org/10.1021/acsnano.6b05691