HUMAN VACCINES & IMMUNOTHERAPEUTICS
2025, VOL. 21, NO. 1, 2472493
https://doi.org/10.1080/21645515.2025.2472493

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS Check for updates

Global research progress in antibody-drug conjugates for solid tumors: Bibliometrics and visualized analysis

Wenjun Fang[a*], Xueqing Ma[b*], and Ben Liu[c,d]

[a]Department of Pharmacy, The Affiliated Yancheng Maternity & Child Health Hospital of Yangzhou University, Yancheng, China; [b]Department of Dermatology, The Affiliated Yancheng Maternity & Child Health Hospital of Yangzhou University, Yancheng, China; [c]Yancheng No.1 People's Hospital, Affiliated Hospital of Medical School, Nanjing University, Yancheng, China; [d]Pediatric Intensive Care Unit, The First People's Hospital of Yancheng, Yancheng, China

ABSTRACT

Recently, the use of antibody-drug conjugates (ADCs) in the research and management of solid tumors has increased, making them a key focus in the field of oncology. In this study, we performed a comprehensive literature review of ADCs use in solid tumor treatment. We retrieved data from the Web of Science Core Collection (WoSCC). Following literature retrieval, we conducted a thorough bibliometric and knowledge-mapping analysis of the collected articles. There was a rapid growth in the number of annual publications in this field. The United States had the highest publication volumes and led ADC research for solid tumors. Additionally, The Dana-Farber Cancer Institute had the highest output, and G. Curigliano was identified as the most productive author. The journal "*Cancers*" led in the publishing of ADC research on solid tumors. Furthermore, key clustering terms such as "breast cancer," "targeted therapy," "bladder cancer," "ovarian cancer," "expression," and "drug delivery" emerged in this field as the research progressed. We identified six key themes by literature co-citation analysis, involving the research on the application of four ADCs in breast cancer, as well as the analysis of ADCs design, mechanisms, and strategies for reducing cytotoxicity. At the same time, based on the analysis of papers that have experienced a citation burst recently, we explored the future development trends of this field. Overall, our inaugural bibliometric analysis of ADCs for solid tumor research provides a systematic framework to guide future studies in this field. Therefore, facilitating and promoting further development in this area.

ARTICLE HISTORY
Received 22 September 2024
Revised 14 February 2025
Accepted 22 February 2025

KEYWORDS
Antibody-drug conjugates; ADCs; solid tumors; breast cancer; visual analysis; developing trends

Introduction

Antibody-drug conjugates (ADCs) are a targeted therapeutic approach that integrates the specificity of monoclonal antibodies with the potency of cytotoxic agents connected by linkers. This approach combines the benefit of the accurate targeting capabilities of monoclonal antibodies and the efficacy of cytotoxic drugs.[1,2] ADCs were incorporated into cancer research in the 1980s. Gemtuzumab ozogamicin, an ADC that targets CD33, became the first to be approved by the US Food and Drug Administration (FDA) for commercial use, in 2000.[3] Initially, it was approved for treating acute myeloid leukemia that was either resistant or had relapsed. However, due to its insignificant clinical efficacy and obvious side effects, gemtuzumab ozogamicin was voluntarily withdrawn by the pharmaceutical company.[4,5] In 2011, the FDA approved the second-generation ADC brentuximab vedotin, which targets CD30, for treating Hodgkin's and relapsed systemic anaplastic large-cell lymphoma.[6] Notably, research on ADCs for solid tumors began relatively late, compared with hematological tumors. In 2013, after the withdrawal of gemtuzumab ozogamicin, the FDA approved the first ADC drug for solid tumors, trastuzumab emtansine. This agent specifically targeted patients with HER2 (human epidermal growth factor receptor 2)-positive breast cancer.[7] Moreover, attention to ADCs in the field of solid tumor treatment increased significantly, after achieving this milestone. By August 2024, eight ADCs specifically targeting solid tumors had been approved for clinical use globally (Table 1).[8]

Bibliometrics, which is a thorough and unbiased approach to scientific data analysis, is beneficial to explore the knowledge architecture, developmental trajectories, hotspots, trends, and the contributions of various researchers, institutions, and countries.[9–11] To date, there has been no bibliometric research in the field of ADCs for solid tumors. Therefore, we conducted a bibliometric analysis of ADCs for solid tumors and constructed the corresponding visualization charts to fill this gap.

Materials and methods

Data collection and search strategies

We extracted research data from the Web of Science Core Collection (WoSCC) database on August 2, 2024, following the retrieval and screening methods detailed in Appendix 1 and Figure 1. We used terms related to "ADC" and "solid

CONTACT Ben Liu liuben@ycsyy.com Yancheng No.1 People's Hospital, Affiliated Hospital of Medical School, Nanjing University, 6 South Renmin Road, Yancheng 224000, China.

*These authors contributed equally to this work and shared the first authorship.

Supplemental data for this article can be accessed on the publisher's website at https://doi.org/10.1080/21645515.2025.2472493

Table 1. Summary of antibody-drug conjugates approved for clinical use of solid tumors as of August 2024.

Drugs	Product	Target	Linker	Payload	DAR	Indications	Approved Date
Trastuzumab emtansine	Kadcyla	HER2	SMCC	DM1	3.5	HER2-positive breast cancer	2013/02 FDA/ EMA/PMDA/ NMPA
Enfortumab vedotin	Padcev	Nectin-4	Val-Cit dipeptide	MMAE	3.8	Uroepithelial tumor	2019/12 FDA
Trastuzumab deruxtecan	Enhertu	HER2	GGFG tetrapeptide	DXd	8	HER2-positive breast cancer, gastric or gastresophageal junction adenocarcinoma	2019/12 FDA/ EMA/PMDA
Sacituzumab govitecan	Trodelvy	Trop-2	CL2A	SN38	7.6	Triple-negative breast cancer	2020/04 FDA
Cetuximab sarotalocan	Akalux	EGFR	NA	IRDye700DX	NA	Head and neck tumors	2020/09 PMDA
Disitamab Vedotin	Aidixi	HER2	Val-Cit dipeptide	MMAE	4	HER2 overexpression in locally advanced or metastatic gastric cancer	2021/06 NMPA
Tisotumab vedotin	Tivdak	TF	Val-Cit dipeptide	MMAE	4	Recurrent or metastatic cervical cancer during or after chemotherapy	2021/09 FDA
Mirvetuximab soravtansine	Elahere	FRα	Sulfo-SPDB	DM4	3.4	FRα-positive,drug-resistant epithelial ovarian or fallopian tube or primary peritoneal cancer	2022/11 FDA

HER2, human epidermal growth factor receptor 2; Nectin-4, nectin cell adhesion molecule-4; Trop-2, tumor-associated calcium signal transducer 2; EGFR, epidermal growth factor receptor; TF, tissue factor; FRα, folate receptor alpha; DM1, emtansine; MMAE, monomethyl auristatin E; Dxd, deruxtecan; SN38, 7-ethyl-10-hydroxycamptothecin; FDA, Food and Drug Administration; PMDA, Pharmaceuticals and Medical Devices Agency; NMPA, National Medical Products Administration; EMA, European Medicines Agency.

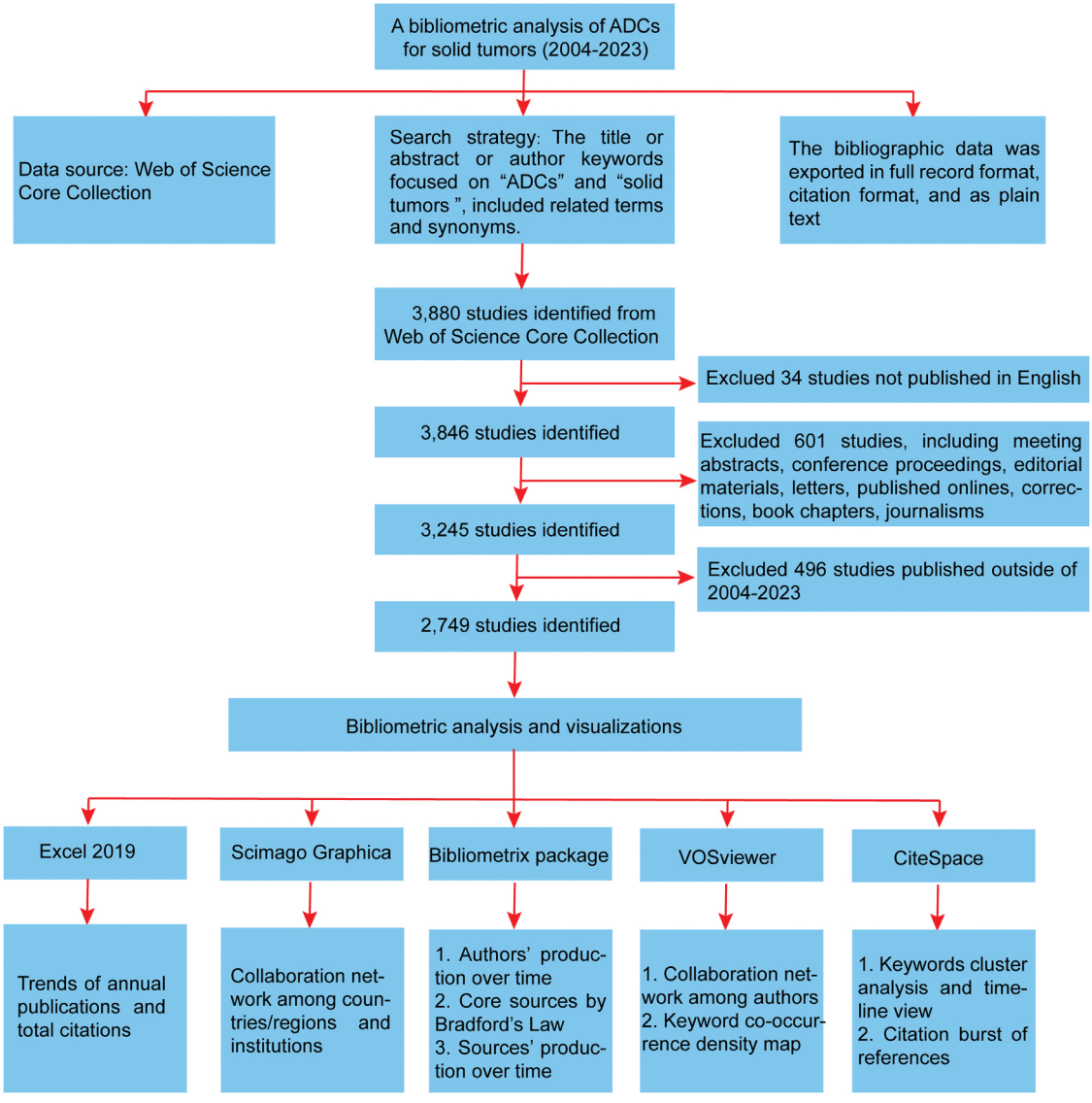

Figure 1. The flow diagram of literature enrollment and data screening.

tumor" and their synonyms as search terms, connecting them with the Boolean operators "OR" and "AND" to conduct a literature search (Appendix 1). Researchers Wenjun Fang and Xueqing Ma screened the retrieved literature and excluded irrelevant ones (such as those related to hematological ADCs). In case of any disagreements during the screening process, the two resolved them through thorough discussions. Finally, a total of 2,749 papers were retrieved.

Data analysis

We used tools such as R package Bibliometrix, CiteSpace (version 6.3.R3), VOSviewer (version 1.6.19), Scimago Graphica (version 1.0.44), and Microsoft Office Excel 2019 to manage, analyze, and visualize the data. Bibliometrix, a comprehensive bibliometric research tool developed in R, facilitated the entire process, from gathering data to generating visual representations.[12] Additionally, we used CiteSpace and VOSviewer, which are Java-based software for bibliometric analysis and visualization, each with their unique strengths. CiteSpace helps uncover and examine latent information within the literature, whereas VOSviewer has robust visualization features.[13] Notably, Scimago Graphica is a data visualization tool that does not require coding. Furthermore, a more diverse range of visualization effects can be achieved by importing the data generated by VOSviewer.[14]

Results

Analysis of publication trends

The number of publications and citations increased between 2004 and 2023, with 2023 marking the peak year. In 2023, 559 papers were published, with a total number of citations exceeding 20,000 (Figure 2). Notably, as of August 2, 2024 (the data download date), 369 related papers had been published in 2024. Based on this publication trajectory, the expected total number of publications for the entirety of 2024 is expected to sustain an upward trend.

Analysis of countries/regions and institutions

We analyzed the publications from 77 nations and 3,865 institutions. The analysis revealed that the United States (US) led with 1,341 (48.78%), followed by China (501, 18.22%), Italy (253, 9.20%), Japan (216, 7.86%), and Germany (184, 6.69%) (Table 2). Figure 3 shows the close collaboration among various countries. The US (total link strength of 1,056), positioned at the center, had the connections, highlighting its outstanding contributions to the field. Moreover, the diagram reveals that cooperation between European and American countries is particularly frequent.

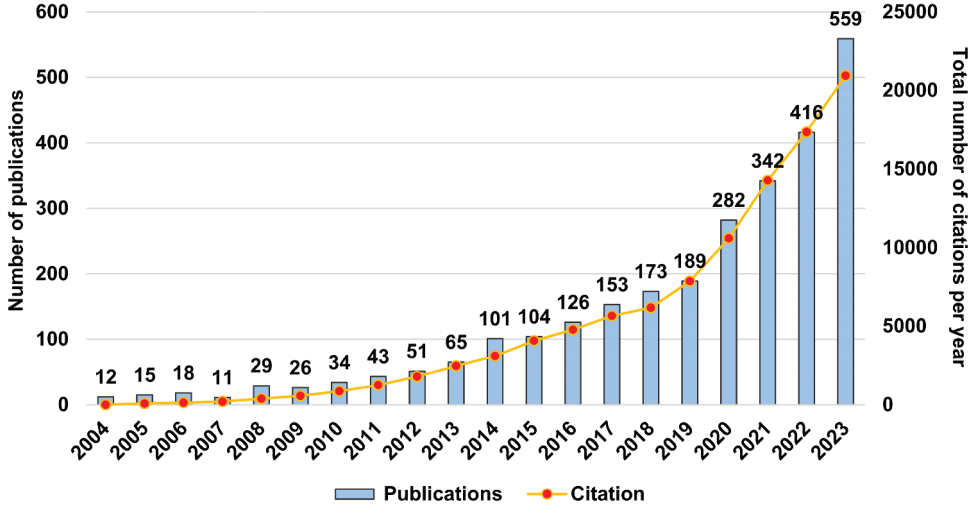

Figure 2. Annual output and citation counts of publications on antibody-drug conjugates for solid tumors from 2004 to 2023.

Table 2. Ranking of the top 10 countries/regions that have published the most articles from 2004 to 2023.

Rank	Country	Count	Proportion (%)	Total link strength
1	USA	1341	48.78	1056
2	China	501	18.22	260
3	Italy	253	9.20	504
4	Japan	216	7.86	261
5	Germany	184	6.69	404
6	Spain	154	5.60	435
7	France	151	5.49	390
8	UK	149	5.42	380
9	Canada	123	4.47	186
10	South Korea	106	3.86	211

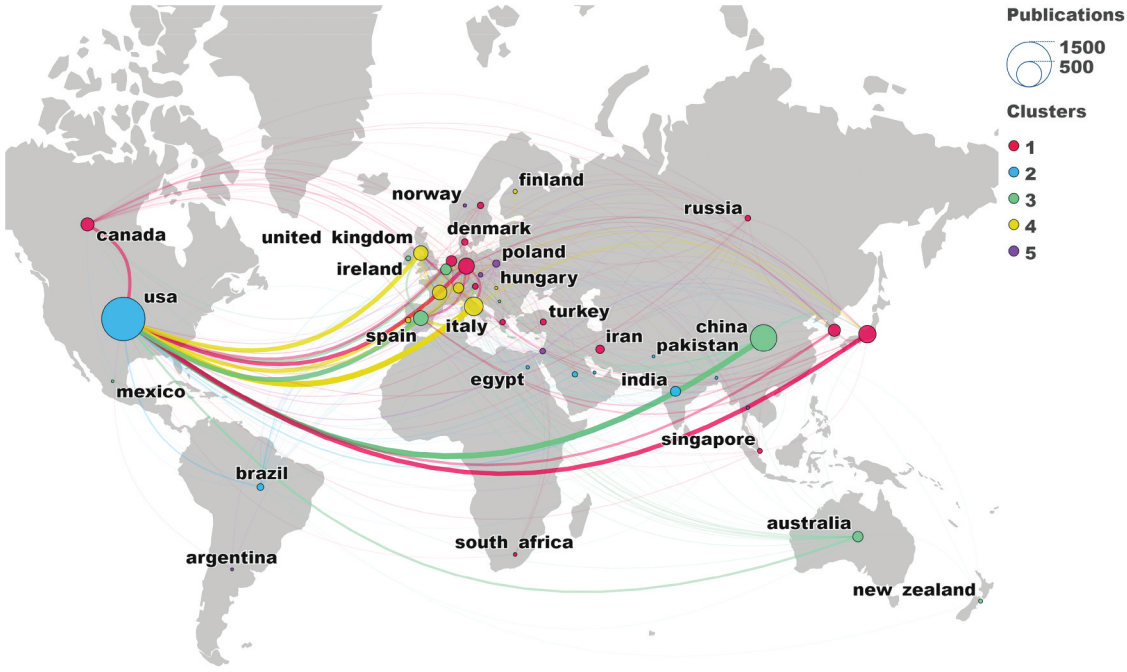

Figure 3. Cooperation network among countries on antibody-drug conjugates for solid tumors from 2004 to 2023.

Table 3. Ranking of the top 10 institutions that have published the most articles from 2004 to 2023.

Rank	Institution	Count	Proportion (%)	Country	Total link strength
1	Dana-Farber Cancer Institute	112	4.07	USA	935
2	Memorial Sloan-Kettering Cancer Center	99	3.60	USA	805
3	Harvard Medical School	97	3.53	USA	527
4	UT MD Anderson Cancer Center	85	3.09	USA	614
5	Genentech Inc.	74	2.69	USA	357
6	University of Milan	66	2.40	Italy	416
7	National Cancer Center	57	2.07	South Korea	386
8	National Cancer Institute	54	1.96	USA	303
9	Massachusetts General Hospital	52	1.89	USA	443
10	University Of California San Francisco	51	1.86	USA	382

Globally, 3,865 research institutions have significantly contributed to advancing the understanding of ADCs in solid tumor research by publishing articles. Notably, the Dana-Farber Cancer Institute had the highest contributions with 112 publications, with a total link strength of 935. It was followed closely by the Memorial Sloan-Kettering Cancer Center, with 99 publications (total link strength of 805), and Harvard Medical School, with 97 publications (total link strength of 527) (Table 3). Of the 10 institutions with the highest contributions, eight are located in the US. We clearly observed the collaborative networks and contributions formed by institutions in this research field by visually analyzing the relevant data (Appendix 2).

Analysis of authors

In total 17,629 authors have contributed to this research field. Curigliano G from the University of Milan and Bardia A from the Massachusetts General Hospital made the most contributions, publishing 39 and 32 papers respectively (Table 4). Overall, Krop IE, from the Dana – Farber Cancer Institute, amassed 7,717 citations. Followed by Goldenberg DM, who

Table 4. Ranking of the top 10 most productive authors and most co-cited authors from 2004 to 2023.

Rank	Author	Count	Citations	Total link strength	Co-cited Author	Citations	Total link strength
1	Curigliano G	39	1495	77	Modi S	808	32055
2	Bardia A	32	2913	90	Bardia A	673	28517
3	Goldenberg DM	28	3789	78	Krop IE	577	23585
4	Tolaney SM	28	2714	87	Slamon DJ	548	20166
5	Cortes J	26	3194	102	Verma S	483	17763
6	Rugo HS	25	2724	82	Ogitani Y	387	15739
7	Tarantino P	23	663	54	Baselga J	385	16567
8	Krop IE	22	7717	64	Phillips GD	357	11976
9	Girish SR	18	2441	60	Powles T	354	12681
10	Govindan SV	18	1922	50	Schmid P	333	16077

was affiliated with the Center for Molecular Medicine and Immunology in Mendham, New Jersey, USA, with 3,789 citations. Furthermore, Modi S from Memorial Sloan Kettering Cancer Center had the most co-citations (808), highlighting their influence on ADCs research in solid tumors. Appendix 3A shows the growth of key academic teams, with notable collaborations by Bardia A, Goldenberg DM, and Cortes J. Moreover, Appendix 3B clearly shows how the authors' publication output and citation frequency evolved over time. Goldenberg and Govindan have authored scholarly articles on the utilization of ADCs for solid tumor therapy since 2009. Notably, Curigliano only began publishing research articles in this field within the last 5 years; however, he had the highest number of publications in the domain. Additionally, the publication volume by Curigliano G peaked between 2022 and 2023, including the highest number of citations for these papers.

Analysis of journals

Academic journals play a crucial role in disseminating scientific research findings. Of the 2,749 publications analyzed, 610 academic journals were identified. The top 10 journals mainly focused on the fields of Clinical Oncology and Molecular Pharmacology (Table 5). The cumulative number of papers published in the field of solid-tumor ADCs by these ten journals was 591, accounting for 21.50% of the total number of papers. *Cancers* led with 117 articles, followed by *Molecular Cancer Therapeutics* with 112, and *Clinical Cancer Research* with 80. The most cited articles were *Clinical Cancer Research* (5,980), *Journal of Clinical Oncology* (5,505), and *Molecular Cancer Therapeutics* (4,524). Additionally, among the top 10 leading journals, 6 are based in the US, and by analyzing the Journal Citation Reports (JCR) quartiles, we can evaluate their quality, with Table 5 showing that 90% of these top 10 journals are in JCR quartile 1 (Q1). Regarding the impact factor, four journals exceeded a score of 10 points. Notably, Bradford's law reveals that, in any given field of study, academic journals can be categorized into three areas based on their significance and relevance: core, secondary, and peripheral areas. The number of journals in the core area was relatively small. These journals concentrated mainly on the key literature in the field. The shaded area in Appendix 4A indicates the main journals in the field of ADCs for solid tumors, highlighting their central position in this discipline. Furthermore, Appendix 4B presents the publication trends in the top five journals over the past two decades. In this field, *Molecular Cancer Therapeutics* maintained a leading position in the number of publications since 2015. However, it was surpassed by *Cancers* after the year 2022.

Analysis of keywords

The keywords reveal the core themes and focal points of academic articles. Overall, 4,243 keywords were identified, with the five most frequently occurring keywords including "ADCs (762)," "breast cancer (380)," "target therapy (220)," "human epidermal growth factor receptor 2 (HER2) (208)," and "immunotherapy (186)" (Table 6). In addition, regarding solid tumors, "breast cancer ($n = 380$)" had the highest occurrence, with a significant co-occurrence frequency. "Triple-negative breast cancer (TNBC) (96)" also had a relatively high frequency of occurrence, ranking second. This was followed by, "ovarian cancer ($n = 69$)" and "non-small cell lung cancer ($n = 60$) occupying the third and fourth positions, respectively. Additionally, keywords that appeared at least 15 times were selected and utilized to create a density map

Table 5. Ranking of the top 10 most productive journals from 2004 to 2023.

Rank	Journal	Article count	Country/ Region	Journal Citation Reports (2023)	Impact Factor (2023)	Total number of citations	Total link strength
1	Cancers	117	Switzerland	Q1	4.5	2145	1122
2	Molecular Cancer Therapeutics	112	USA	Q1	5.3	4524	1302
3	Clinical Cancer Research	80	USA	Q1	10.0	5980	1299
4	Frontiers in Oncology	50	Switzerland	Q2	3.5	675	350
5	International Journal of Molecular Sciences	47	USA	Q1	4.9	827	408
6	Cancer Research	40	USA	Q1	12.5	3975	609
7	Molecular Pharmaceutics	39	USA	Q1	4.5	1567	144
8	Journal of Controlled Release	38	Netherlands	Q1	10.5	2874	135
9	Journal of Clinical Oncology	35	USA	Q1	42.1	5505	1221
10	Scientific Reports	33	England	Q1	3.8	682	142

Table 6. Top 20 keywords about this research field from 2004 to 2023.

Rank	Keywords	Count	Rank	Keywords	Count
1	ADCs (antibody-drug conjugates)	762	11	drug delivery	74
2	breast cancer	380	12	EGFR (epidermal growth factor receptor)	71
3	target therapy	220	13	HER2-low	70
4	HER-2 (human epidermalgrowth factor receptor-2)	208	14	trastuzumab deruxtecan	70
5	immunotherapy	186	15	ovarian cancer	69
6	T-DM1 (trastuzumab emtansine)	142	16	antibodies	68
7	trastuzumab	105	17	checkpoint inhibitors	63
8	TNBC (triple negative breast cancer)	96	18	sacituzumab govitecan	63
9	monoclonal antibodies	93	19	NSCLC (non-small-cell lung cancer)	60
10	cancer	90	20	Trop-2 (trophoblast surface antigen 2)	60

(Appendix 5), offering a more graphical depiction. Subsequently, a keyword co-occurrence analysis was performed, which clustered the keywords and showed the progression of research trends and focal points (Appendix 6). The identified clusters were labeled as follows: #0, drug delivery; #1, breast cancer; #2, ovarian cancer; #3, targeted therapy; #4, expression; and #5, bladder cancer.

Analysis of references

Appendix 7 presents the 10 leading papers with the most co-citations in this research field. Notably, the co-citation frequencies of these papers exceeded 100. Of these papers, "Trastuzumab deruxtecan in previously treated HER2-positive breast cancer (298)"[15] and "Trastuzumab deruxtecan in previously treated HER2-low advanced breast cancer (196)"[16] were first and second in terms of co-citation frequency. Additionally, these papers were authored by Modi S and published in the *New England Journal of Medicine* in 2020 and 2022, respectively.

In academic research, citation bursts refer to a situation where some literature receives a large number of citations far exceeding the average level of its peers within a short period. This often indicates the formation of current academic hotspots. After all, only those works that touch upon the academic forefront and present innovative concepts or methods can be widely cited in a short time. Conducting in-depth analysis of these works helps to understand the direction of academic research, gain insights into future trends, and provide strong guidance for subsequent research.[17] In Appendix 8, we identified 261 documents that had this citation trend. Of these, 60 (22.99%) showed a continuous citation burst with no signs of decline, indicating that these papers have been widely noticed and frequently cited by the academic community in recent years. Additionally, the publication years of these papers ranged from 2017–2021, with 20 published in or after 2020. These publications included 18 articles, one correspondence, and one session abstract. Based on the citation burst intensity of these papers, we conducted a detailed classification, summarization, and in-depth analysis of 18 noteworthy papers (Appendix 9).

Discussion

General information

Since the approval of the first ADC (trastuzumab emtansine) targeting solid tumors in 2013, the number of research studies in this field has witnessed a substantial increase, suggesting an increasing interest in leveraging ADCs as a therapeutic approach for solid tumors. In addition, significant progress is expected regarding the use of these drugs for treating solid tumors as ongoing studies explore the intricacies of ADCs and address the obstacles they face. These advancements can potentially benefit individuals with these cancers.

Our findings suggest that the US has contributed significantly to ADC research and development (Table 2), and the trend of increasing collaboration between different countries and institutions in recent years has positively contributed to the development of this field. The FDA is a government agency specifically responsible for regulating food, drugs, cosmetics, and medical devices, and it plays a leading role in the timely approval of drugs.[18] Although the FDA is only an agency within the United States, many regulatory authorities in other countries and regions often refer to the FDA's decisions during the drug approval decision-making process, and in some cases, even follow them directly.[19,20] As shown in Table 1, six of the eight ADC drugs approved globally for the treatment of solid tumors are approved by the FDA.[21]

Compared with Goldenberg DM and Govindan SV, who are regarded as leading researchers in the field, Curigliano G emerged as a prominent researcher in this field, with publication output increasing significantly over the past 5 years, eventually surpassing the aforementioned researchers. Co-citation analysis reveals that the top two most-cited articles are both authored by Modi S, highlighting the pivotal role of their research in the field. Both of these articles focus on the application of trastuzumab deruxtecan in the treatment of breast cancer.

Furthermore, *Cancers*, *Molecular Cancer Therapeutics*, and *Clinical Cancer Research* have significantly focused on ADC research, which is confirmed by the extensive publication of related articles. Our research uncovered a notable phenomenon: beginning in 2004, *Molecular Cancer Therapeutics* and *Clinical Cancer Research* focused on the use of ADCs for solid tumor therapy, and over time, the publication count in this field in both journals increased year-by-year. However, there was a significant surge in publication count regarding ADC research in *Cancers*. This increase allowed *Cancers* to eventually surpass *Molecular Cancer Therapeutics* to become the journal with the most publications in this area. This trend reflected the growing emphasis on ADCs research in the academic community and highlights the significant role of *Cancers* in promoting the development of related research.

Knowledge frameworks and hotspot evolution

Cluster analysis of author keywords related to ADCs for solid tumors (Appendix 6) showed that the current knowledge structure in this field (sorted by time) can be divided into six sub-areas: "breast cancer," "targeted therapy," "bladder cancer," "ovarian cancer," "expression," and "drug delivery." Furthermore, the timeline visualization of keywords effectively illustrates the progression of keywords and associated research themes over time. Within this domain, a significant volume of keywords surfaced at different intervals between 2004 and 2023. The keywords were primarily focused on "antibody therapy," "clinical trials," and "safety" prior to 2013. However, the focus changed when the first-generation ADC was introduced for solid tumors, which was trastuzumab emtansine, in 2013. Evidence revealed that it can be used to treat HER2-positive breast cancer.[22] Subsequently, scientists focused on studying the mechanisms of resistance to ADCs between 2013 and 2019, exploring new targets and combination therapies. Moreover, the field of solid tumor treatment experienced the introduction of various ADCs, significantly increasing the range of available treatments for solid tumors. Therefore, the focus since 2019 has shifted to the emergence of novel ADCs. This

progression in terminology aligns with the historical trajectory of ADC development and reflects the shifts in areas of interest within the field.[23]

We found that seven of the top-10 most co-cited papers (three on HER2-positive breast cancer,[15,24,25] two on HER2-low breast cancer,[16,26] two on TNBC,[27,28] one on solid tumors,[29] and two review articles[30,31] focused on the treatment of breast cancer with ADCs (Appendix 7). Furthermore, among the top 10 most co-cited papers, a variety of ADCs were covered. Specifically, three papers were focused on the study of trastuzumab deruxtecan, two papers explored sacituzumab govitecan, and another two were centered on the analysis of trastuzumab emtansine. Additionally, one study examined the efficacy of trastuzumab duocarmazine.

We comprehensively analyzed the top-10 most co-cited studies and summarized the current key topics in the ADC domain for solid tumors as follows:

(1) The antitumor activity and safety of trastuzumab deruxtecan in various HER2-expressing breast cancers.
(2) Evaluation of efficacy, safety, and prognostic impact of sacituzumab govitecan in patients with triple-negative breast cancer (TNBC).
(3) Efficacy and prognosis of trastuzumab emtansine in advanced invasive HER2-positive breast cancer.
(4) Strategies for selecting the best target antigen and appropriate cytotoxic drugs for ADCs, as well as the design optimization of linkers.
(5) Mechanisms of action, resistance mechanisms, and strategies for mitigating ADC cytotoxicity
(6) Clinical research on trastuzumab duocarmazine for the treatment of locally advanced and metastatic solid tumors and HER2-expressing breast cancer.

The aforementioned topics are important in this field. ADCs are expected to become increasingly instrumental in the management of solid tumors following research in this field.[32]

Future trends

Burst analysis of reference citations reveals future trends in this field. In our analysis of the 18 most frequently cited studies on burst strength (Appendix 9),[33–50] we identified several prominent solid tumor types that are currently in focus, including breast, urothelial, cervical, and gastric cancers. Additionally, we have identified a set of ADCs that are receiving significant attention. These agents include sacituzumab govitecan,[34,39,40,44] enfortumab vedotin,[35,43] trastuzumab deruxtecan,[37,38,47] and tisotumab vedotin.[48] The particularly prominent targets in the field are HER2, anti-trophoblast cell-surface antigen 2 (Trop-2), nectin cell adhesion molecule-4 (Nectin-4), and tissue factor (TF). Finally, the cytotoxic agents highlighted were 7-Ethyl-10-hydroxycamptothecin (SN38), monomethyl auristatin E (MMAE), and deruxtecan (DXd). Through an in-depth analysis of these documents, we discovered that the mechanisms of action of ADCs, the types of solid tumors they target, the selection of targets and payloads, and their efficacy, safety, and prognosis are prominent topics in the research field. Hence, exploring and optimizing new possibilities for the efficacy of ADCs, improving the understanding of adverse reactions, and managing and mitigating related toxicities are required future development trends in this field of research.[33,41]

Since 2013, a variety of new ADCs targeting solid tumors have been developed and approved for clinical use (Table 1). This is because of the strategic interchange or modification of the antibody, target, linker, and payload in ADCs. Typically, small-scale drug screens are carried out in vitro or in xenograft models to optimize each element of the ADC construct based on a given tumor subtype. These approaches usually focus on comparing a single monoclonal antibody (mAb) modified by a limited selection of linker – payload combinations. Although this strategy is rational, it might overlook opportunities to enhance antibody pharmacodynamics. This is because mAbs directed against the same antigen can have diverse binding characteristics and may influence receptor dimerization or target internalization in distinct ways, potentially leading to considerable differences in their biological effects within the body.[31] Although ADCs hold great promise in targeted cancer therapy, they still face challenges in terms of off-target toxicity control, and resistance management.[51] Bispecific ADCs offer a new treatment strategy for cancer treatment, because they can bind to different molecular targets and are connected to cytotoxic drugs via cleavable or non-cleavable linkers, thereby enhancing tumor specificity and promoting antigen internalization, and reducing off-target toxicity.[52] Compared with monospecific antibodies, bispecific antibodies have several advantages, including the ability to circumvent drug resistance, as well as enhanced internalization and specificity. These characteristics contribute to improving the efficacy and safety of ADCs.[53,54] For example, BL-B01D1 is a conjugate of a tetravalent bispecific antibody targeting HER3 and epidermal growth factor receptor, a cleavable linker, and a topoisomerase I inhibitor. BL-B01D1 exerts its action through two key processes. First, via endocytosis, it penetrates cells, unleashes DNA-damaging agents, and eliminates tumor cells. Second, it impedes the formation of EGFR-HER3 heterodimers, thus curbing downstream cell-growth signals. In a Phase I clinical trial involving 195 patients with locally advanced or metastatic solid tumors, researchers found that BL-B01D1 demonstrated preliminary anti-tumor activity in heavily pretreated advanced solid tumors, and its safety profile was acceptable.[55] Unfortunately, no bispecific ADCs have been approved to date, and a large number of clinical trials are still needed to prove their efficacy and safety.[56]

There is an abundance of innovative potential for selecting effective payloads for ADCs. This encompasses the transition from conventional cytotoxic medications to specifically selected targeted treatments or immunotherapies that are chosen for their capacity to suppress tumor cell activity. For example, mirzotamab clezutoclax is an ADC that targets B7-H3 (CD276) and has a proapoptotic BCL-XL inhibitor as its payload. It is currently under investigation in the initial phases of clinical trials.[57] Moreover, cutting-edge ADCs integrate immunostimulatory substances, such as Toll-like receptor activators, stimulators of interferon gene (STING) agonists, or chemokines. Their purpose is to attract and/or energize

immune cells to focus on tumor-related antigens, thereby boosting the anti-cancer response.[31] In addition to single-payload ADC drugs, recently, researchers have developed a novel dual-payload ADC that targets CD276. This drug was proven to be effective against TNBC and showed low toxicity in various mouse models. Currently, this dual-payload ADC is still undergoing evaluation for its therapeutic effects.[58] The research on effective payloads has provided new directions for the development of ADCs, providing more effective treatment options for cancer therapy.

Newer generations of ADCs exhibit reduced cytotoxicity compared with their earlier counterparts; however, the adverse reactions associated with ADCs pose a significant challenge. Therefore, beyond drug design and preclinical studies, it falls upon clinical and translational researchers to investigate the clinical potential of ADCs through well-considered clinical trial designs. This work has two aspects. First, it involves improving predictive biomarkers to clarify the indications for ADC use. This can help patients without indications avoid unnecessary toxicity.[59] Furthermore, biomarkers are used to identify patients suitable for targeted therapies during clinical trials. Immunohistochemistry (IHC) is the main technique for assessing the presence of specific proteins. However, IHC can provide semi-quantitative analysis results. Hence, currently, there is no unified clear basis for determining the criteria for positive judgment, with different studies possibly adopting different cutoff values. This means that IHC is a useful tool; however, its limitations in quantification need to be supplemented by other methods or more precise techniques to ensure the accuracy and reliability of clinical trials.[60] Second, explore potential synergistic treatments with ADCs to enhance their clinical efficacy. Notably, various studies have focused on ADCs with other therapeutic approaches and different mechanisms of action with the aim of reducing the occurrence of drug resistance, delaying the development of resistance, and enhancing the overall therapeutic benefit.[61,62] For example, the simultaneous use of the pan-HER inhibitor neratinib with ADCs that target HER2 can lead to the internalization of the antigen, thereby enhancing the endocytosis and efficacy of ADCs.[63] Therefore, enhancing our understanding and application of the intricate interactions between ADCs and tumors could reveal the full potential of this therapeutic approach, potentially transforming solid tumor treatment for patients.[64]

Conclusion

In recent years, there have been significant advancements in the field of ADCs for solid tumors. In this study, we used bibliometric methods to comprehensively organize and analyze the literature in this area. We systematically examined key indicators such as the number of related papers, countries and institutions of the authors, journals in which they were published, citation patterns, and frequently cited documents. In this study, detailed statistical data were provided, including an in-depth analytical discussion. Furthermore, we identified six areas of interest in the field and predicted future development trends. These findings provide a significant reference value for scholars focusing on the study of ADCs in solid tumors.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The author(s) reported there is no funding associated with the work featured in this article.

Notes on contributor

Ben Liu, an attending physician in the Pediatric Intensive Care Unit at Yancheng First People's Hospital, is also pursuing a graduate degree at Nanjing University Medical School. He currently serves as a committee member of the Critical Care and Neurology Groups of the Yancheng Medical Association's Pediatric Branch, as well as a committee member of the Yancheng Nutrition Society. He specializes in the research of pediatric critical illnesses and pediatric neurophysiology, and the application of bibliometrics analysis and meta-analysis.

ORCID

Ben Liu http://orcid.org/0000-0002-0574-2455

Author contributions

W.F.: Writing-Original draft preparation, manuscript, investigation, and figure preparation. X.M.: manuscript, investigation, and figure preparation. B.L.: Conceptualization, Methodology, Supervision.

Data availability statement

The data presented in this study are available on request from the corresponding author.

Ethics statement

This study did not involve human or animal subjects and therefore did not require formal ethical approval. All research activities were conducted in accordance with ethical standards for research without direct human or animal participation.

References

1. Parit S, Manchare A, Gholap AD, Mundhe P, Hatvate N, Rojekar S, Patravale V. Antibody-drug conjugates: a promising breakthrough in cancer therapy. Int J Pharm. 2024;659:124211. doi:10.1016/j.ijpharm.2024.124211.
2. Chis AA, Dobrea CM, Arseniu AM, Frum A, Rus L-L, Cormos G, Georgescu C, Morgovan C, Butuca A, Gligor FG, et al. Antibody–drug conjugates—evolution and perspectives. Int J Mol Sci. 2024;25(13):6969. doi:10.3390/ijms25136969.
3. Liu K, Li M, Li Y, Li Y, Chen Z, Tang Y, Yang M, Deng G, Liu H. A review of the clinical efficacy of fda-approved antibody–drug conjugates in human cancers. Mol Cancer. 2024;23(1):62. doi:10.1186/s12943-024-01963-7.
4. Tsuchikama K, Anami Y, Ha SYY, Yamazaki CM. Exploring the next generation of antibody–drug conjugates. Nat Rev Clin Oncol. 2024;21(3):203–223. doi:10.1038/s41571-023-00850-2.
5. Selby C, Yacko LR, Glode AE. Gemtuzumab Ozogamicin: back again. J Adv Pract Oncol. 2019;10(1):68–82. doi:10.6004/jadpro.2019.10.1.6.
6. Song CH, Jeong M, In H, Kim JH, Lin CW, Han KH. Trends in the development of antibody-drug conjugates for cancer therapy. Antibodies (Basel). 2023;12(4):72. doi:10.3390/antib12040072.

7. Filis P, Zerdes I, Soumala T, Matikas A, Foukakis T. The ever-expanding landscape of antibody-drug conjugates (ADCs) in solid tumors: a systematic review. Crit Rev Oncol Hematol. 2023;192:104189. doi:10.1016/j.critrevonc.2023.104189.
8. Ruan DY, Wu HX, Meng Q, Xu RH. Development of antibody-drug conjugates in cancer: overview and prospects. Cancer Commun (Lond). 2024;44(1):3–22. doi:10.1002/cac2.12517.
9. Miao L, Zhang J, Xu W, Qian Q, Zhang G, Yuan Q, Lv Y, Zhang H, Shen C, Wang W. Global research trends in CAR-T cell therapy for solid tumors: a comprehensive visualization and bibliometric study (2012–2023). Hum Vaccin Immunother. 2012–2023;20 (1):2338984. doi:10.1080/21645515.2024.2338984.
10. Liang J, Lin Y, Liu Y, Lin H, Xie Z, Wu T, Zhang X, Zhou X, Tan Z, Yin W, et al. Deciphering two decades of cellular reprogramming in cancer: a bibliometric analysis of evolving trends and research frontiers. Heliyon. 2024;10(11):e31400. doi:10.1016/j.heliyon.2024.e31400.
11. Lythgoe MP, Lewison G, Aggarwal A, Booth C, Lawler M, Trapani D, Sengar M, Sullivan R. The rise of immuno-oncology in China: a challenge to western dominance? Lancet Oncol. 2023;24(5):439–441. doi:10.1016/S1470-2045(23)00026-8.
12. Huang Y, Hu R, Wu L, He K, Ma R. Immunoregulation of Glia after spinal cord injury: a bibliometric analysis. Front Immunol. 2024;15:1402349. doi:10.3389/fimmu.2024.1402349.
13. Tang S, Hao R, Liu X, He H, Tian Y, Jing T, Liu Z, Xu Y, Li X. Global trends in Cryptococcus and its interactions with the host immune system: a bibliometric analysis. Front Immunol. 2024;15:1397338. doi:10.3389/fimmu.2024.1397338.
14. Ma X, Deng K, Sun Y, Wu M. Research trends on cancer neuroscience: a bibliometric and visualized analysis. Front Neurosci. 2024;18:1408306. doi:10.3389/fnins.2024.1408306.
15. Modi S, Saura C, Yamashita T, Park YH, Kim S-B, Tamura K, Andre F, Iwata H, Ito Y, Tsurutani J, et al. Trastuzumab deruxtecan in Previously treated HER2-positive breast cancer. N Engl J Med. 2020;382(7):610–621. doi:10.1056/NEJMoa1914510.
16. Modi S, Jacot W, Yamashita T, Sohn J, Vidal M, Tokunaga E, Tsurutani J, Ueno NT, Prat A, Chae YS, et al. Trastuzumab deruxtecan in Previously treated HER2-low advanced breast cancer. N Engl J Med. 2022;387(1):9–20. doi:10.1056/NEJMoa2203690.
17. Amjad T, Shahid N, Daud A, Khatoon A. Citation burst prediction in a bibliometric network. Scientometrics. 2022;127(5):2773–2790. doi:10.1007/s11192-022-04344-3.
18. Gloy V, Schmitt AM, Düblin P, Hirt J, Axfors C, Kuk H, Pereira TV, Locher C, Caquelin L, Walter-Claudi M, et al. The evidence base of US food and drug administration approvals of novel cancer therapies from 2000 to 2020. Int J Cancer. 2023;152 (12):2474–2484. doi:10.1002/ijc.34473.
19. Lythgoe MP, Sullivan R. Outsourcing UK regulatory decisions—a double-edged sword? Lancet. 2023;402(10395):24–25. doi:10.1016/S0140-6736(23)01132-7.
20. Durán CE, Cañás M, Urtasun MA, Elseviers M, Andia T, Vander Stichele R, Christiaens T. Regulatory reliance to approve new medicinal products in Latin American and Caribbean countries. Rev Panam Salud Publica. 2021;45:1–10. doi:10.26633/RPSP.2021.10.
21. Lythgoe MP, Desai A, Gyawali B, Savage P, Krell J, Warner JL, Khaki AR. Cancer therapy approval timings, review speed, and publication of pivotal registration trials in the US and Europe, 2010–2019. JAMA Netw Open. 2022;5(6):e2216183. doi:10.1001/jamanetworkopen.2022.16183.
22. Jaime-Casas S, Barragan-Carrillo R, Tripathi A. Antibody-drug conjugates in solid tumors: a new frontier. Curr Opin Oncol. 2024;36(5):421–429. doi:10.1097/CCO.0000000000001064.
23. Li JH, Liu L, Zhao XH. Precision targeting in oncology: The future of conjugated drugs. Biomed & Pharmacother = Biomedecine & Pharmacotherapie. 2024;177:117106. doi:10.1016/j.biopha.2024.117106.
24. von Minckwitz G, Huang CS, Mano MS, Loibl S, Mamounas EP, Untch M, Wolmark N, Rastogi P, Schneeweiss A, Redondo A, et al. Trastuzumab emtansine for residual invasive HER2-positive breast cancer. N Engl J Med. 2019;380(7):617–628. doi:10.1056/NEJMoa1814017.
25. Verma S, Miles D, Gianni L, Krop IE, Welslau M, Baselga J, Pegram M, Oh D-Y, Diéras V, Guardino E, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer. N Engl J Med. 2012;367(19):1783–1791. doi:10.1056/NEJMoa1209124.
26. Modi S, Park H, Murthy RK, Iwata H, Tamura K, Tsurutani J, Moreno-Aspitia A, Doi T, Sagara Y, Redfern C, et al. Antitumor activity and safety of trastuzumab deruxtecan in patients with HER2-low–Expressing advanced breast cancer: results from a phase Ib study. J Clin Oncol. 2020;38(17):1887–1896. doi:10.1200/JCO.19.02318.
27. Bardia A, Hurvitz SA, Tolaney SM, Loirat D, Punie K, Oliveira M, Brufsky A, Sardesai SD, Kalinsky K, Zelnak AB, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. N Engl J Med. 2021;384(16):1529–1541. doi:10.1056/NEJMoa2028485.
28. Bardia A, Mayer IA, Vahdat LT, Tolaney SM, Isakoff SJ, Diamond JR, O'Shaughnessy J, Moroose RL, Santin AD, Abramson VG, et al. Sacituzumab Govitecan-hziy in Refractory Metastatic Triple-Negative Breast Cancer. N Engl J Med. 2019;380 (8):741–751. doi:10.1056/NEJMoa1814213.
29. Banerji U, van Herpen CML, Saura C, Thistlethwaite F, Lord S, Moreno V, Macpherson IR, Boni V, Rolfo C, de Vries EGE, et al. Trastuzumab duocarmazine in locally advanced and metastatic solid tumours and HER2-expressing breast cancer: a phase 1 dose-escalation and dose-expansion study. Lancet Oncol. 2019;20 (8):1124–1135. doi:10.1016/S1470-2045(19)30328-6.
30. Beck A, Goetsch L, Dumontet C, Corvaïa N. Strategies and challenges for the next generation of antibody-drug conjugates. Nat Rev Drug Discov. 2017;16(5):315–337. doi:10.1038/nrd.2016.268.
31. Drago JZ, Modi S, Chandarlapaty S. Unlocking the potential of antibody–drug conjugates for cancer therapy. Nat Rev Clin Oncol. 2021;18(6):327–344. doi:10.1038/s41571-021-00470-8.
32. Fu Z, Li S, Han S, Shi C, Zhang Y. Antibody drug conjugate: the "biological missile" for targeted cancer therapy. Signal Transduct Target Ther. 2022;7(1):93. doi:10.1038/s41392-022-00947-7.
33. Nagayama A, Vidula N, Ellisen L, Bardia A. Novel antibody-drug conjugates for triple negative breast cancer. Ther Adv Med Oncol. 2020;12:1758835920915980. doi:10.1177/1758835920915980.
34. Kalinsky K, Diamond JR, Vahdat LT, Tolaney SM, Juric D, O'Shaughnessy J, Moroose RL, Mayer IA, Abramson VG, Goldenberg DM, et al. Sacituzumab govitecan in previously treated hormone receptor-positive/HER2-negative metastatic breast cancer: final results from a phase I/II, single-arm, basket trial. Ann Oncol. 2020;31(12):1709–1718. doi:10.1016/j.annonc.2020.09.004.
35. Rosenberg J, Sridhar SS, Zhang J, Smith D, Ruether D, Flaig TW, Baranda J, Lang J, Plimack ER, Sangha R, et al. EV-101: a phase I study of single-agent enfortumab vedotin in patients with nectin-4–Positive solid tumors, including metastatic urothelial carcinoma. J Clin Oncol. 2020;38(10):1041–1049. doi:10.1200/JCO.19.02044.
36. Murthy RK, Loi S, Okines A, Paplomata E, Hamilton E, Hurvitz SA, Lin NU, Borges V, Abramson V, Anders C, et al. Tucatinib, trastuzumab, and capecitabine for HER2-positive metastatic breast cancer. N Engl J Med. 2020;382(7):597–609. doi:10.1056/NEJMoa1914609.
37. Keam SJ. Trastuzumab Deruxtecan: first approval. Drugs. 2020;80 (5):501–508. doi:10.1007/s40265-020-01281-4.
38. Shitara K, Bang YJ, Iwasa S, Sugimoto N, Ryu M-H, Sakai D, Chung H-C, Kawakami H, Yabusaki H, Lee J, et al. Trastuzumab deruxtecan in Previously treated HER2-positive gastric cancer. N Engl J Med. 2020;382(25):2419–2430. doi:10.1056/NEJMoa2004413.
39. Syed YY. Sacituzumab Govitecan: first approval. Drugs. 2020;80 (10):1019–1025. doi:10.1007/s40265-020-01337-5.
40. Rugo HS, Bardia A, Tolaney SM, Arteaga C, Cortes J, Sohn J, Marmé F, Hong Q, Delaney RJ, Hafeez A, et al. TROPiCS-02: a phase III study investigating sacituzumab govitecan in the treatment of HR+/HER2- metastatic breast cancer. Future Oncol. 2020;16(12):705–715. doi:10.2217/fon-2020-0163.

41. Boni V, Sharma MR, Patnaik A. The resurgence of antibody drug conjugates in cancer therapeutics: novel targets and payloads. Am Soc Clin Oncol Educ Book. 2020;40(40):1–17. doi:10.1200/EDBK_281107.
42. Powles T, Park SH, Voog E, Caserta C, Valderrama BP, Gurney H, Kalofonos H, Radulović S, Demey W, Ullén A, et al. Avelumab maintenance therapy for advanced or metastatic urothelial carcinoma. N Engl J Med. 2020;383(13):1218–1230. doi:10.1056/NEJMoa2002788.
43. Chang E, Weinstock C, Zhang L, Charlab R, Dorff SE, Gong Y, Hsu V, Li F, Ricks TK, Song P, et al. FDA approval summary: enfortumab vedotin for locally advanced or metastatic urothelial carcinoma. Clin Cancer Res. 2021;27(4):922–927. doi:10.1158/1078-0432.CCR-20-2275.
44. Goldenberg DM, Sharkey RM. Sacituzumab govitecan, a novel, third-generation, antibody-drug conjugate (ADC) for cancer therapy. Expert Opin Biol Ther. 2020;20(8):871–885. doi:10.1080/14712598.2020.1757067.
45. Schmid P, Abraham J, Chan S, Wheatley D, Brunt AM, Nemsadze G, Baird RD, Park YH, Hall PS, Perren T, et al. Capivasertib plus paclitaxel versus placebo plus paclitaxel as first-line therapy for metastatic triple-negative breast cancer: the PAKT trial. JCO. 2020;38(5):423–433. doi:10.1200/JCO.19.00368.
46. Schmid P, Cortes J, Pusztai L, McArthur H, Kümmel S, Bergh J, Denkert C, Park YH, Hui R, Harbeck N, et al. Pembrolizumab for early triple-negative breast cancer. N Engl J Med. 2020;382(9):810–821. doi:10.1056/NEJMoa1910549.
47. Tsurutani J, Iwata H, Krop I, Jänne PA, Doi T, Takahashi S, Park H, Redfern C, Tamura K, Wise-Draper TM, et al. Targeting HER2 with Trastuzumab Deruxtecan: a dose-expansion, phase I study in multiple advanced solid tumors. Cancer Discov. 2020;10(5):688–701. doi:10.1158/2159-8290.CD-19-1014.
48. Hong DS, Concin N, Vergote I, de Bono JS, Slomovitz BM, Drew Y, Arkenau H-T, Machiels J-P, Spicer JF, Jones R, et al. Tisotumab Vedotin in Previously treated recurrent or metastatic cervical cancer. Clin Cancer Res. 2020;26(6):1220–1228. doi:10.1158/1078-0432.CCR-19-2962.
49. Lin NU, Borges V, Anders C, Murthy RK, Paplomata E, Hamilton E, Hurvitz S, Loi S, Okines A, Abramson V, et al. Intracranial efficacy and survival with tucatinib plus trastuzumab and capecitabine for Previously treated HER2-positive breast cancer with brain metastases in the HER2CLIMB trial. JCO. 2020;38(23):2610–2619. doi:10.1200/JCO.20.00775.
50. Swain SM, Miles D, Kim SB, Im Y-H, Im S-A, Semiglazov V, Ciruelos E, Schneeweiss A, Loi S, Monturus E, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA): end-of-study results from a double-blind, randomised, placebo-controlled, phase 3 study. Lancet Oncol. 2020;21(4):519–530. doi:10.1016/S1470-2045(19)30863-0.
51. Wolska-Washer A, Robak T. Safety and tolerability of antibody-drug conjugates in cancer. Drug Saf. 2019;42(2):295–314. doi:10.1007/s40264-018-0775-7.
52. Suurs FV, Lub-de Hooge MN, de Vries EGE, de Groot DJA. A review of bispecific antibodies and antibody constructs in oncology and clinical challenges. Pharmacol Ther. 2019;201:103–119. doi:10.1016/j.pharmthera.2019.04.006.
53. Cui X, Jia H, Xin H, Zhang L, Chen S, Xia S, Li X, Xu W, Chen X, Feng Y, et al. A novel bispecific antibody targeting PD-L1 and VEGF with combined anti-tumor activities. Front Immunol. 2021;12:778978. doi:10.3389/fimmu.2021.778978.
54. Neijssen J, Cardoso RMF, Chevalier KM, Wiegman L, Valerius T, Anderson GM, Moores SL, Schuurman J, Parren PWHI, Strohl WR, et al. Discovery of amivantamab (JNJ-61186372), a bispecific antibody targeting EGFR and MET. J Biol Chem. 2021;296:100641. doi:10.1016/j.jbc.2021.100641.
55. Ma Y, Huang Y, Zhao Y, Zhao S, Xue J, Yang Y, Fang W, Guo Y, Han Y, Yang K, et al. BL-B01D1, a first-in-class EGFR–HER3 bispecific antibody–drug conjugate, in patients with locally advanced or metastatic solid tumours: a first-in-human, open-label, multicentre, phase 1 study. Lancet Oncol. 2024;25(7):901–911. doi:10.1016/S1470-2045(24)00159-1.
56. Zeng H, Ning W, Liu X, Luo W, Xia N. Unlocking the potential of bispecific ADCs for targeted cancer therapy. Front Med. 2024;18(4):597–621. doi:10.1007/s11684-024-1072-8.
57. Perets R, Dowlati A, LoRusso P, Yonemori K, He L, Munasinghe W, Noorani B, Johnson EF, Zugazagoitia J. Mirzotamab clezutoclax as monotherapy and in combination with taxane therapy in relapsed/refractory solid tumors: dose expansion results. J Clin Oncol. 2023 June 1. Published online. doi:10.1200/JCO.2023.41.16_suppl.3027.
58. Zhou Z, Si Y, Zhang J, Chen K, George A, Kim S, Zhou L, Liu X". A dual-payload antibody–drug conjugate targeting CD276/B7-H3 elicits cytotoxicity and immune activation in triple-negative breast cancer. Cancer Res. 2024 Aug 26;84(22):3848–3863. Published online. doi:10.1158/0008-5472.CAN-23-4099.
59. Bijelić A, Silovski T, Mlinarić M, Čipak Gašparović A. Peroxiporins in triple-negative breast cancer: biomarker potential and therapeutic perspectives. Int J Mol Sci. 2024;25(12):6658. doi:10.3390/ijms25126658.
60. Mebratie DY, Dagnaw GG. Review of immunohistochemistry techniques: applications, current status, and future perspectives. Semin Diagn Pathol. 2024;41(3):154–160. doi:10.1053/j.semdp.2024.05.001.
61. Yu P, Zhu C, You X, Gu W, Wang X, Wang Y, Bu R, Wang K. The combination of immune checkpoint inhibitors and antibody-drug conjugates in the treatment of urogenital tumors: a review insights from phase 2 and 3 studies. Cell Death Dis. 2024;15(6):433. doi:10.1038/s41419-024-06837-w.
62. Wei Q, Li P, Yang T, Zhu J, Sun L, Zhang Z, Wang L, Tian X, Chen J, Hu C, et al. The promise and challenges of combination therapies with antibody-drug conjugates in solid tumors. J Hematol Oncol. 2024;17(1):1. doi:10.1186/s13045-023-01509-2.
63. Li BT, Michelini F, Misale S, Cocco E, Baldino L, Cai Y, Shifman S, Tu H-Y, Myers ML, Xu C, et al. HER2-mediated internalization of cytotoxic agents in ERBB2 amplified or mutant lung cancers. Cancer Discov. 2020;10(5):674–687. doi:10.1158/2159-8290.CD-20-0215.
64. Cheng X, Sun Y, Highkin M, Vemalapally N, Jin X, Zhou B, Prior JL, Tipton AR, Li S, Iliuk A, et al. Breast cancer mutations HER2V777L and PIK3CAH1047R activate the p21–CDK4/6–cyclin D1 axis to drive tumorigenesis and drug resistance. Cancer Res. 2023;83(17):2839–2857. doi:10.1158/0008-5472.CAN-22-3558.