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Review of US- based cost effectiveness evaluations for Antibody Drug Conjugates (ADCs) in oncology

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INTRODUCTION

- Antibody-drug conjugates (ADCs) are a class of biopharmaceuticals that utilize monoclonal antibodies to selectively deliver potent cytotoxic agents to the tumor site.[1]
- They are structured as an antibody conjugated with a linker to a cytotoxic payload, thus combining the targeting ability of a monoclonal antibody with a potent cytotoxic effect to efficiently eliminate cancer cells.[1]
- ADCs have evolved significantly in recent years for multiple disease areas, especially cancer. The first ADC was approved by the FDA (Food and Drug Administration) in 2000; since then, another 14 ADCs have gained approval for a variety of indications.[1]
- However, ADCs are associated with high costs due to novelty and complexity of development, which may hinder their accessibility.
- In the current changing treatment landscape, it is important to understand how cost-effective the ADCs are compared to the other therapies available in the market for cancer.

OBJECTIVES

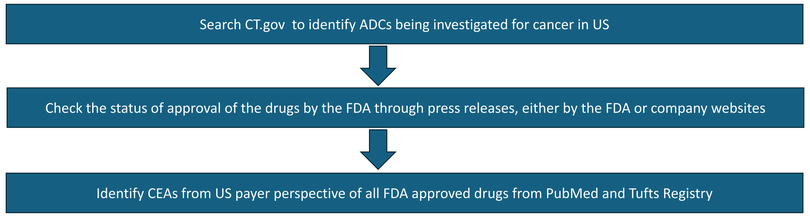
This review aimed:

- To identify ADCs approved for oncology by the FDA
- To review the US-based cost-effectiveness evaluations (CEAs) for these ADCs

METHODS

- We used clinicaltrials.gov (CT.gov) to identify trials investigating ADCs in oncology, primarily in the US, and analyzed their trial status. We also verified their status of drug development through press releases, either by FDA or the company websites.
- Subsequently, CEA for all FDA-approved ADCs were also identified and reviewed. (Figure 1)

Figure 1: Flow chart depicting methods followed for identifying ADCs and their CEAs



RESULTS

SECTION A: Trial characteristics

- CT.gov provided 242 hits, from which 66 ADCs were identified. 49 of them were phase I/II trials, while 17 were in phase III. Primary disease areas targeted by identified ADCs were lung cancer, breast cancer, and lymphoma (Figure 2). 11 ADCs have received FDA approval since 2011. Additionally, 8 ADCs have received Orphan Drug Designation (ODD) only, 10 ADCs have received Fast Track/Breakthrough designations, and 5 ADCs received both designations (Table 1).

Figure 2: Disease indications identified and phases of studies

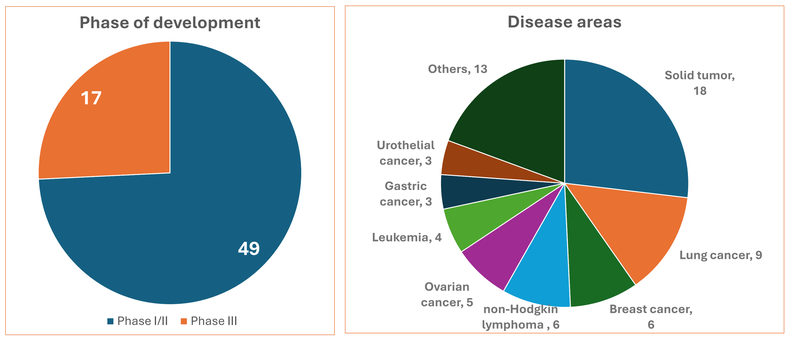


Table 1: FDA designations received by different ADCs

FDA Designation			
1. ODD	Brentuximab Vedotin (BV), Gemtuzumab Ozogamicin (GO), Inotuzumab Ozogamicin (IO), Loncastuximab Tesirine (LT), Polatuzumab Vedotin (PV)	**4. Accelerated Approval**	EV, LT, Mecbotamab Vedotin (MV), Mirvetuximab Soravtansine (MS), TD, Tisotumab Vedotin (TV)
2. Fast Track/ Breakthrough	BV, Enfortumab Vedotin (EV), IO, Trastuzumab Deruxtecan (TD), Trastuzumab Emtansine (TE)	**5. Priority Review**	BV, EV, IO, LT, MS, SG, TV, TD, TE, GO
3. CRL	Sacituzumab Govitecan (SG)	**6. Assessment Aid**	SG, LT, TV, TD, EV, BV

SECTION B: Description of approved ADCs

Table 2: Description of 11 ADCs

ADC, Year of first approval	Target	Cytotoxic payload	Disease indication
Brentuximab vedotin, 2011	CD30 antigen	Monomethyl auristatin E (MMAE)	Hodgkins's lymphoma Systemic anaplastic large cell lymphoma Primary cutaneous anaplastic large cell lymphoma Large B-cell lymphoma
Enfortumab vedotin, 2019	Nectin 4	Monomethyl auristatin E (MMAE)	Urothelial cancer
Gemtuzumab ozogamicin, 2017	CD33 antigen	Calicheamicin	Acute myeloid leukaemia
Inotuzumab ozogamicin, 2017	CD22 protein	N-acetyl-γ-calicheamicin	Acute lymphoblastic leukaemia
Loncastuximab tesirine, 2021	CD19 protein	Pyrrolobenzodiazepine (PBD) dimer, SG3199	Diffuse large B-cell lymphoma
Mirvetuximab Soravtansine, 2022	Folate receptor alpha	DM4	Ovarian, fallopian tube, or primary peritoneal cancer
Polatuzumab vedotin, 2019	CD79b	Monomethyl auristatin E (MMAE)	Diffuse large B-cell lymphoma
Sacituzumab govitecan, 2020	Trophoblast cell-surface antigen 2 (Trop-2)	SN-38	Breast cancer
Tisotumab vedotin, 2021	Tissue factor expressing tumors	Monomethyl auristatin E (MMAE)	Cervical cancer
Trastuzumab deruxtecan, 2019	HER2 receptor	Deruxtecan (DXd)	Breast cancer Non-small cell lung cancer Gastric cancer Other solid tumors
Trastuzumab emtansine, 2013	HER2 receptor	Emtansine (DM1)	Breast cancer

SECTION C: CEAs identified

- Search on PubMed and Tufts registry provided us with 29 publications for the 11 ADCs. (Table 3)

Table 3: CEAs on the 11 ADCs

	Sr. No.	Author, year	Drug name	Comparator	Costs year	WTP	QALY gained	ICER
ADC vs ADC	1	Mudumba et al. 2024[2]	Trastuzumab deruxtecan	Trastuzumab emtansine	2022	$100,000/QALY	5.09	$230,285/QALY
	2	Yang et al. 2022[3]	Trastuzumab deruxtecan	Trastuzumab emtansine	2022	$150,000/QALY	3.83	$82,112/QALY
	3	Zhu et al. 2022[4]	Trastuzumab deruxtecan	Trastuzumab emtansine	2021	$150,000/QALY	4.354	$13,342/QALY
Immunotherapies vs ADC	4	Delea et al. 2019[5]	Blinatumomab	Inotuzumab Ozogamicin	2018	$150,000/QALY	0.54-1.78	$4,006-$20,737/QALY
	5	Large et al. 2018[6]	Pembrolizumab	Brentuximab vedotin	2017	$20,000/QALY	0.5	Dominant (cost saving)
ADC vs Chemotherapy	6	Huo et al., 2024[7]	Tisotumab vedotin	Chemotherapy	2023	$150,000/QALY	0.25	$839,107/QALY
	7	Wu et al. 2021[8]	Enfortumab vedotin	Chemotherapy	2021	$150,000/QALY	0.69	$2,168,746/QALY
	8	Li et al. 2024[9]	Enfortumab vedotin	Chemotherapy	2024	$150,000/QALY	3.254	$558,973/QALY
	9	Zhu et al. 2024[10]	Enfortumab vedotin	Chemotherapy	2024	$150,000/QALY	1.1	$267,491/QALY
	10	Zhu et al. 2024[11]	Mirvetuximab soravtansine	Chemotherapy	2023	$100,000/QALY	0.9	$596,189/QALY
	11	Shi et al. 2023[12]	Trastuzumab deruxtecan	Chemotherapy	2021	$100,000/QALY	0.727	$83,892/QALY
	12	Lang et al. 2022[13]	Trastuzumab deruxtecan	Chemotherapy	2021	$150,000/QALY	1.487	$346,571/QALY
	13	Yang et al. 2023[14]	Trastuzumab deruxtecan	Chemotherapy	2022	$150,000/QALY	0.47	$317,494/QALY
	14	Zhu et al. 2022[15]	Trastuzumab deruxtecan	Chemotherapy	2022	$150,000/QALY	1.869	$296,873/QALY
	15	Xie et al. 2023[16]	Sacituzumab govitecan	Chemotherapy	2023	$150,000/QALY	0.7297	$1,252,295/QALY
	16	Lang et al. 2023[17]	Sacituzumab govitecan	Chemotherapy	2023	$150,000/QALY	0.781	$778,771/QALY
	17	Chen et al. 2021[18]	Sacituzumab govitecan	Chemotherapy	2021	$150,000/QALY	0.87	$494,479/QALY
	18	Shi et al. 2023[19]	Sacituzumab govitecan	Chemotherapy	2023	$150,000/QALY	1.766	$612,772/QALY
ADC vs targeted therapy	19	Filho et al. 2022[20]	Ado-Trastuzumab Emtansine	Trastuzumab	2018	$180,000/QALY	0.45	$11,467/QALY

Table 3: CEAs on the 11 ADCs (continued)

	Sr. No.	Author, year	Drug name	Comparator	Costs year	WTP	QALY gained	ICER
ADC vs Combination therapies	20	Richardson et al. 2023[21]	Tisotumab vedotin	Chemotherapy + bevacizumab + pembrolizumab	NR	$150,000/QALY and $300,000/ QALY	1.422	$320,072.99 (CER)
	21	Quang A. Le, 2016[22]	Trastuzumab Emtansine	Lapatinib + capecitabine , monotherapy capecitabine	2015	$150,000/QALY	NR	TE vs Lapatinib + capecitabine: $220,385/QALY TE vs capecitabine monotherapy: $168,355/QALY
	22	Matasar et al. 2023[23]	Polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone (Pola-R-CHP)	Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP)	2023	$150,000/QALY	10.15	$88,855/QALY
	23	Betts et al. 2020[24]	Polatuzumab vedotin, bendamustine and rituximab (Pola-BR)	Bendamustine and rituximab (BR)	2020	$150,000/QALY	3.31	$35,864/QALY
	24	Kambhampati et al. 2022[25]	Polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone (Pola-R-CHP)	Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP)	2021	$150,000/QALY	11.8	$84,308/QALY
	25	Calamia et al, 2021[26]	Tafasitamab-lenalidomide (Tafa-L)	Polatuzumab vedotin-bendamustin-rituximab (PBR)	2021	$150,000/QALY	1.7	$310,041/QALY
	26	Huntington et al. 2017[27]	Brentuximab vedotin + (doxorubicin, vinblastine, and dacarbazine)	Bleomycin containing chemotherapy (doxorubicin, bleomycin, vinblastine, and dacarbazine)	2017	$150,000/QALY	0.56	$317,254/QALY
	27	Delea et al. 2018[28]	Brentuximab vedotin + (doxorubicin, vinblastine, and dacarbazine (A + AVD)	Doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD)	2018	$100,000–$200,000/QALY	0.76	$172,074/QALY
	28	Cai et al, 2025[29]	Trastuzumab Deruxtecan	Docetaxel, Nivolumab	2024	$150,000/QALY	1.16, 0.53, 1.10	$338,997.84/QALY(T-DXd vs Docetaxel), $1,437,258.33/QALY (T-DXd vs Nivolumab)
ADC vs Observation	29	Hui et al. 2017[30]	Brentuximab vedotin	Active surveillance	2016	$100,000/QALY	1.07	$148,664/QALY

KEY INSIGHTS

- This review identified 11 ADCs that are FDA approved indicating superior efficacy of ADCs across multiple disease areas as of 20th December 2024.
- The identified CEAs consistently show that ADCs at current price are not cost-effective compared to most drug classes, especially immunotherapies and chemotherapies, which could be due to high drug acquisition cost of ADCs. It was observed that reducing the cost, improvement in quality of life and focusing on clinically responsive groups to strengthen value for money could bring the ICERs within the WTP threshold. However, the suggested range of price reduction varied widely (5-80%) across ADCs and disease areas.
- Alternatively, assessing cost-effectiveness in terms of Equal Value of Life Years Gained (evLYG) which estimates the actual value of a healthy life year irrespective of disability or illness could be beneficial.
- Even though most ADCs were not found to be cost-effective, their coverage could have been predominantly driven by clinical benefit and price negotiations. However, we could not account for the commercially confidential discounts due to the lack of data.
- A key approach to balancing innovation with affordability for ADCs involves establishing fair pricing agreements and expanding insurance coverage. These efforts should be supported by cost-effectiveness evaluations and alternative payment models.

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