A Review of NICE UK Submissions for Antibody-Drug Conjugates in Oncology

Barinder Singh[2], Ritesh Dubey[1], Gagandeep Kaur[1], Sumeet Attri[1]

[1]Pharmacoevidence, SAS Nagar Mohali, India; [2]Pharmacoevidence, London, UK

HTA70

Pharmaco® Evidence

CONCLUSION

Antibody-drug conjugates (ADCs) have revolutionized cancer treatment with their targeted delivery and significant therapeutic benefits. The evolution of ADCs since the 2000s highlights their potential in both refractory and early-stage diseases. Continued advancements in ADC design and technology promise even greater therapeutic efficacy. The future of ADCs looks bright, with innovations poised to further enhance their clinical impact

INTRODUCTION

- Antibody-drug conjugates (ADCs) represent a novel therapeutic modality in oncology, combining the specificity of monoclonal antibodies (mAbs) with the potent cytotoxicity of chemotherapeutic agents [1]
- By linking cytotoxic payloads to mAbs via covalent bonds, ADCs are designed to selectively target and destroy tumor cells that express specific surface antigens, aiming to minimize off-target toxicity and improve the therapeutic index [1]
- ADCs have gained significant clinical traction, with multiple FDA-approved agents now available for the treatment of various malignancies including breast cancer, lymphomas, and urothelial carcinoma [2]
- These therapies mark a paradigm shift in precision oncology, offering new treatment options where traditional chemotherapy may fall short in efficacy or tolerability [3]
- As ADCs become more integrated into clinical practice, it is important to understand how health technology assessment (HTA) bodies, such as the National Institute for Health and Care Excellence (NICE) in the UK, evaluate and recommend these treatments

OBJECTIVE

- To identify and analyze the US Food and Drug Administration (FDA)-approved ADCs that have been submitted to NICE for appraisal
- This includes summarizing their therapeutic indications, appraisal outcomes, and key clinical and economic considerations within NICE submissions

METHODS

- The NICE technology appraisals were manually searched using relevant keywords from the database inception to December 2024
- All retrieved documents were screened to identify the HTA documents that met pre-specified eligibility criteria as outlined in **Figure 1**
- The evidence screening and extraction of relevant data into data tables was conducted by a single independent reviewer, followed by a quality check by a second independent reviewer

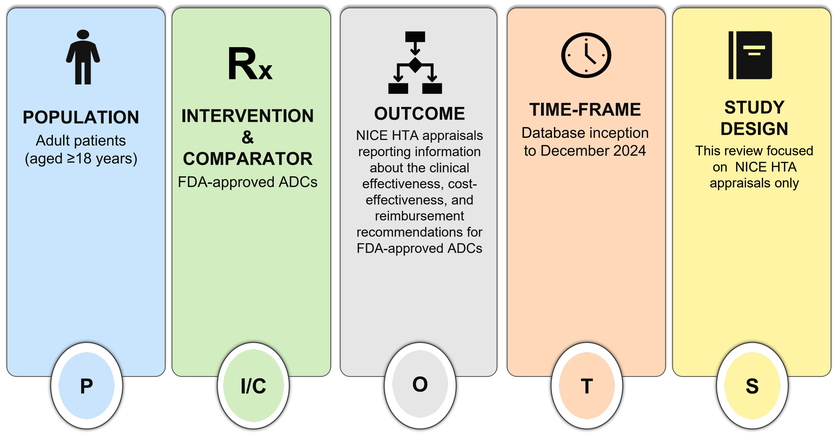
RESULTS

- A total of 150 HTAs were identified, of which 16 HTAs involving 12 FDA-approved ADCs met the pre-specified eligibility criteria
- Of the 16 HTAs, 12 were reimbursed by NICE, while decisions of the remaining four are awaited
- The four ADCs in development at the time of analysis were: tisotumab vedotin (Tivdak) for cervical cancer, enfortumab vedotin (Padcev) for urothelial cancer, mirvetuximab soravtansine-gynx (Elahere) for ovarian cancer, and belantamab mafodotin-blmf (Blenrep) for multiple myeloma
- The ADCs were appraised for the use of various cancer types such as lymphoma (n=6), breast cancer (n=3), and leukemia (n=2)

References

1. Fu, Z., Li, S., Han, S., Shi, C., & Zhang, Y. (2022). Antibody–drug conjugate: the "biological missile" for targeted cancer therapy. Signal Transduction and Targeted Therapy, 7(1), 93.Bandi S et al., Am J Rhinol. Allergy, 34 (4)
2. Gogia, P., Ashraf, H., Bhasin, S., & Xu, Y. (2023). Antibody–drug conjugates: a review of approved drugs and their clinical level of evidence. Cancers, 15(15), 3886
3. Liu, K., Li, M., Li, Y., Li, Y., Chen, Z., Tang, Y., Yang, M., Deng, G., & Liu, H. (2024). A review of the clinical efficacy of FDA-approved antibody–drug conjugates in human cancers. Molecular Cancer, 23, Article 62.

Figure 1: Pre-defined PICOS eligibility criteria



ADC: Antibody-Drug Conjugate; FDA: Food and Drug Administration; HTA: Health Technology Assessment; NICE: National Institute for Health and Care Excellence

RESULTS

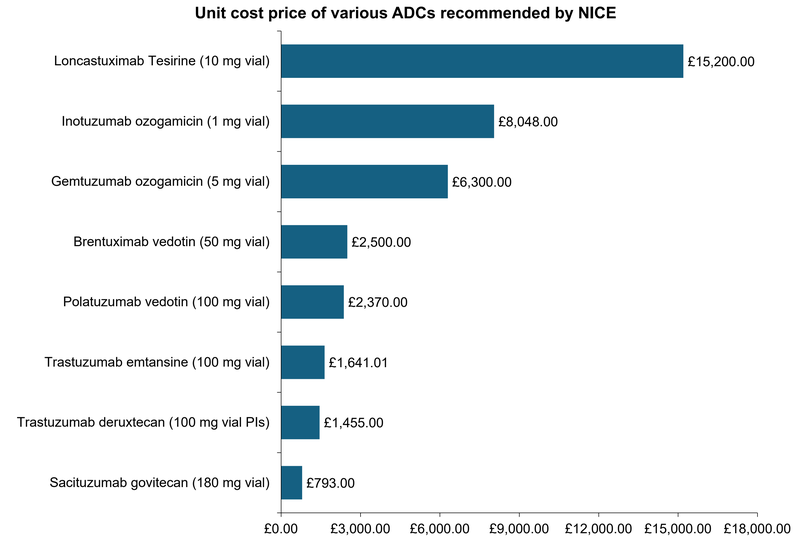
- Three ADCs in combination with chemotherapy were reimbursed by NICE (**Table 1**):
  - Brentuximab vedotin (Adcetris) + chemotherapy for systemic anaplastic large cell lymphoma (sALCL)
  - Polatuzumab vedotin (Polivy) + rituximab, cyclophosphamide, doxorubicin, prednisone (R-CHP) for untreated diffuse large B-cell lymphoma (DLBCL), and
  - Gemtuzumab ozogamicin (Mylotarg) + chemotherapy for CD33-positive acute myeloid leukemia (AML).
- Compared to first-line, ADCs were reimbursed by NICE for use as monotherapy in second or later-line and third-line settings across varied indications (**Table 1**):
  - Brentuximab vedotin (Adcetris) for previously treated patients of ALCL, Hodgkin's lymphoma (HL), and T-cell lymphoma (TCL)
  - Polatuzumab vedotin (Polivy) for relapsed/refractory DLBCL
  - Inotuzumab ozogamicin (Besponsa) for B-cell acute lymphoblastic leukemia (ALL)
  - Sacituzumab govitecan (Trodelvy) for metastatic triple-negative breast cancer (mTNBC)
  - Trastuzumab emtansine (Kadcyla) and Trastuzumab deruxtecan (Enhertu), for HER2-positive breast cancer
- All HTA submissions primarily consisted of randomized controlled trials (RCTs). However, one submission relied on data from a non-RCT (TA524), reflecting either the rarity of the condition or the challenge of conducting head-to-head RCTs in certain patient populations.
- Unit costs for the ADCs ranged from £793 (Trodelvy) to £15,200 (Zynlonta) per vial, depending on the agent, dosage, and formulation **Figure 2**
- Cost-effectiveness evaluations were incorporated in most of the submissions, with analyses conducted using incremental cost-effectiveness ratios (ICERs) and varied willingness-to-pay (WTP) thresholds (range €10,000 to €30,000 per quality-adjusted life year (QALY)

Table 1: Summary of included HTAs and their Recommendation status

Drug Name	Indication	NICE Recommendation	HTA ID
First-line			
Brentuximab vedotin (Adcetris) + CHP (Combo)	ALCL	Recommended	TA1059
Gemtuzumab ozogamicin (Mylotarg) + chemotherapy (Combo)	CD33+ AML	Recommended with condition (cytogenetics, CA)	TA545
Polatuzumab vedotin (Polivy) + R-CHP (Combo)	DLBCL	Recommended with condition (IPI 2–5, CA)	TA874
Second-line or later			
Brentuximab vedotin (Adcetris) (Mono)	ALCL	Recommended with condition (ECOG 0–1, CA)	TA524
	CD30+ HL	Recommended with condition (post-ASCT or 2L unsuitable)	TA524
	Cutaneous TCL	Recommended with condition (CA)	TA577
Inotuzumab ozogamicin (Besponsa) (Mono)	CD22+ B-cell ALL	Recommended with condition (MA, Ph+ needs prior TKI)	TA541
Polatuzumab vedotin (Polivy) (Mono)	Relapsed/refractory DLBCL	Recommended with condition (transplant ineligible, CA)	TA649
Trastuzumab deruxtecan (Enhertu) (Mono)	HER2+ mBC	Recommended with condition (MA/CDF)	TA1026
Trastuzumab emtansine (Kadcyla) (Mono)	HER2+ aBC	Recommended with condition (prior trastuzumab + taxane)	TA458
	HER2+ early BC with residual disease	Recommended	TA632
Third-Line			
Loncastuximab tesirine (Zynlonta) (Mono)	DLBCL or high-grade BCL	Recommended with condition (post-Polatuzumab or unsuitable)	TA947
Sacituzumab govitecan (Trodelvy) (Mono)	Metastatic TNBC	Recommended with condition (≥2 prior, high unmet need)	TA819

ALCL: Anaplastic large cell lymphoma; ALL: Acute lymphoblastic leukemia; APL: Acute promyelocytic leukemia; ASCT: Autologous stem cell transplant; Combo: Recommended as combination; CDF: Cancer Drugs Fund; CHP: Cyclophosphamide, doxorubicin, prednisone; DLBCL: Diffuse large B-cell lymphoma; ECOG: Eastern Cooperative Oncology Group; HL: Hodgkin lymphoma; HER2+: Human epidermal growth factor receptor 2-positive; IPI: International Prognostic Index; MA: Marketing authorization; M: Metastatic; Mono: Recommended as monotherapy; MF: Mycosis fungoides; pcALCL: Primary cutaneous ALCL; Ph+: Philadelphia chromosome-positive; R-CHP: Rituximab, cyclophosphamide, doxorubicin, prednisone; TNBC: Triple-negative breast cancer; TCL: T-cell lymphoma.

Figure 2: Per unit cost of various ADCs recommended by NICE



ADC: Antibody-Drug Conjugate; NICE: National Institute for Health and Care Excellence

For further queries, please contact

Sumeet.Attri@Pharmacoevidence.com