AN EXPLORATORY DIVE INTO THE WORLD OF ANTIBODY DRUG CONJUGATES

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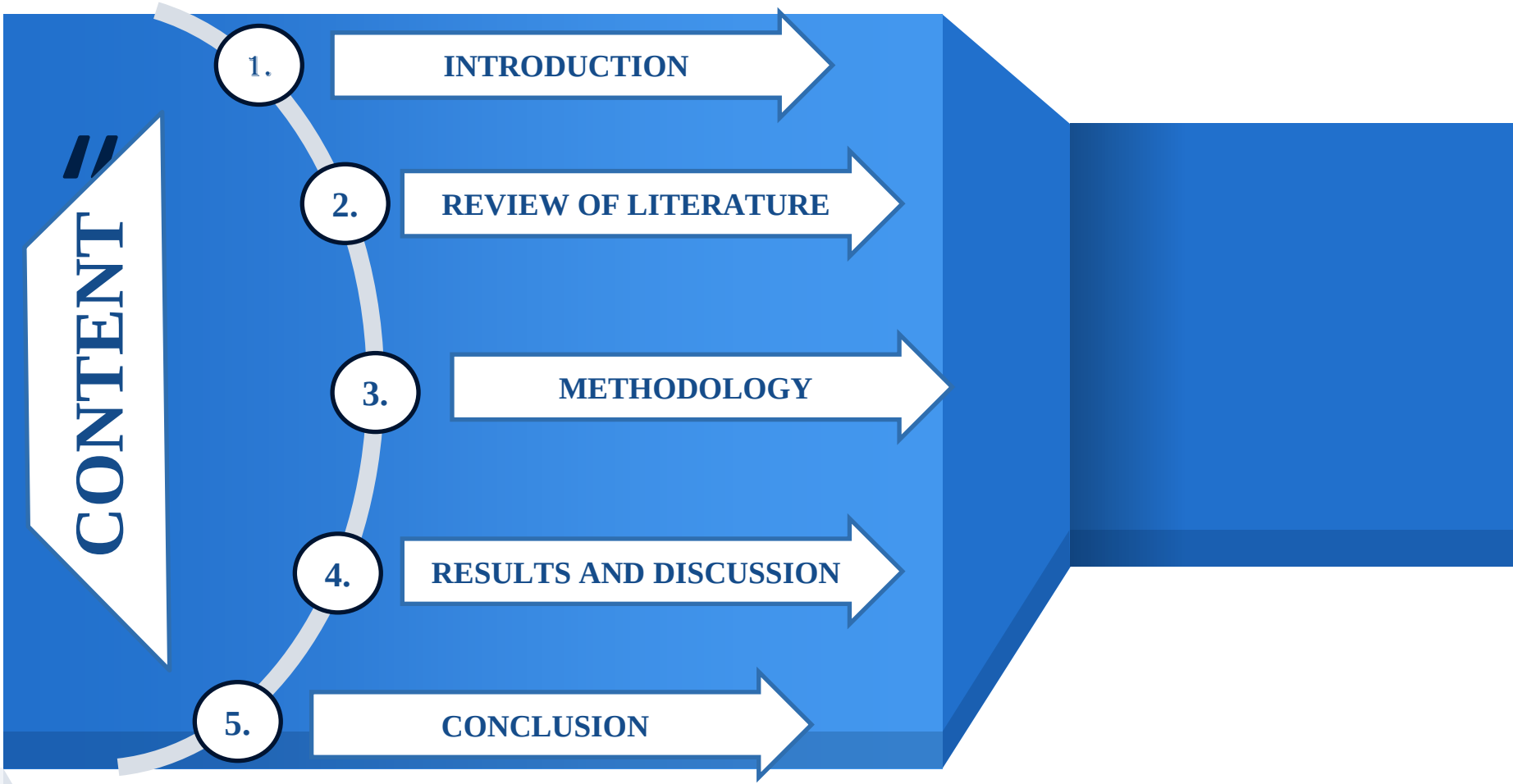
CONTENT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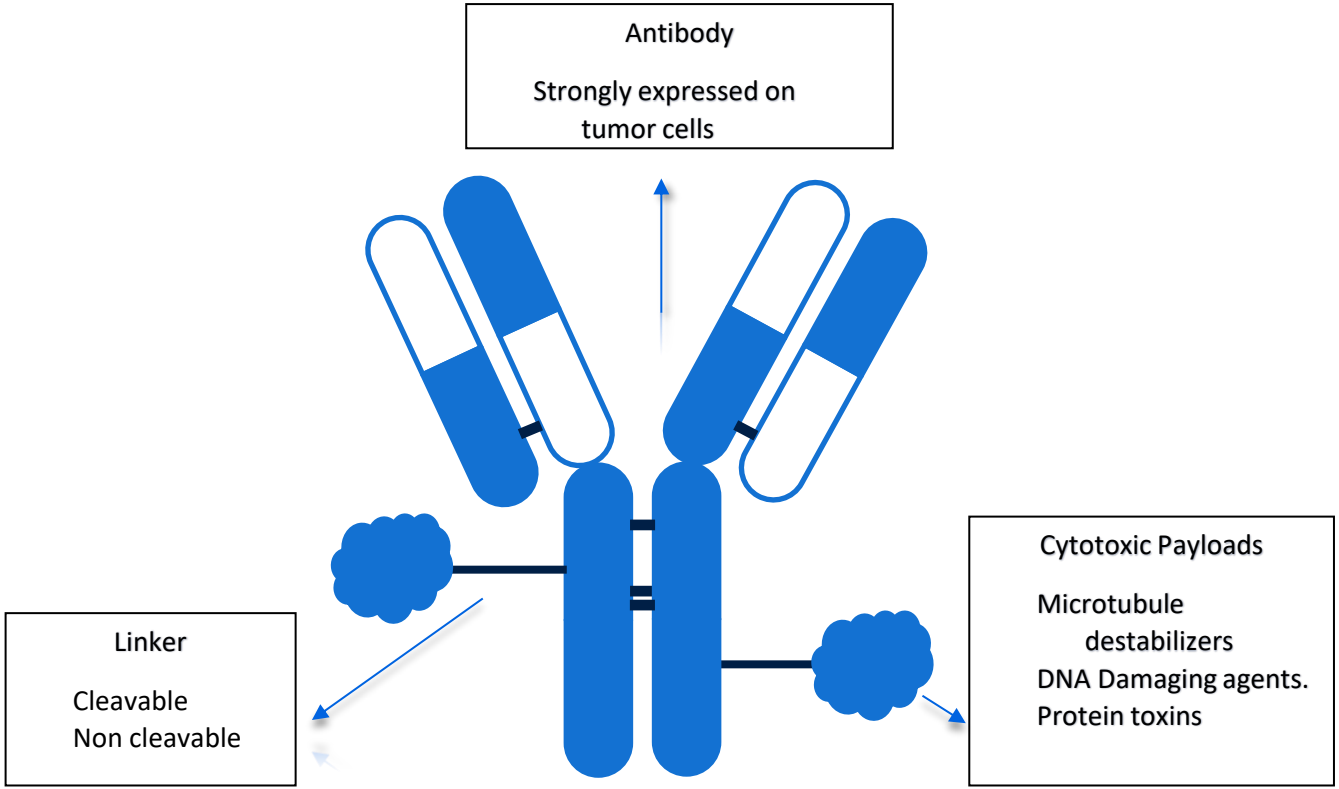
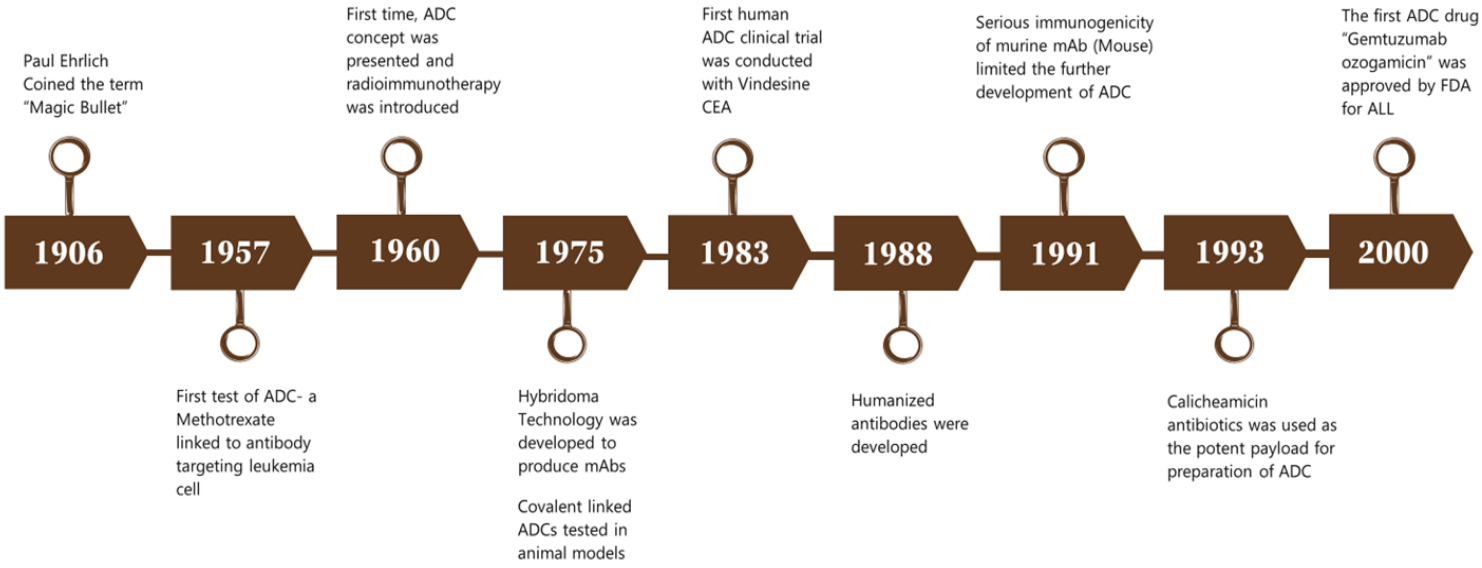
INTRODUCTION

- Antibody-drug conjugates (ADCs) are the new emerging class of biopharmaceuticals who are complex molecules consisting of an antibody linked to a biologically active cytotoxic payload or drug
- These drugs are designed as a targeted therapy for treating disease, but at the moment, ADCs are widely used for the management or treatment of cancer
- Among these, chemotherapy has been the go-to treatment for cancer. However, they have very low therapeutic index despite not only targeting the cancerous cells but also destroys healthy cells in the process
- To address this issue, A novel concept of Antibody drug conjugates has been introduced and conceived



Antibody Drug Conjugate

History of Antibody-Drug Conjugate



Component of ADCs

Antibody

- The antibody is the key component in the design of an ADC as targets specific antigens on cancer cells, ensuring precise delivery of the cytotoxic drug to these cells.
- This targeting minimizes damage to healthy cells and enhances the overall efficacy and safety of the treatment.

Linkers

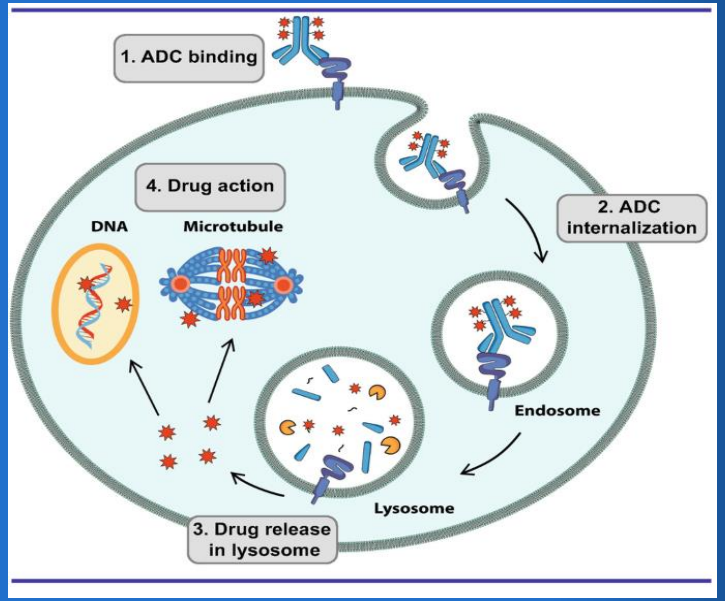
- Linker connects the monoclonal antibody (mAb) to the cytotoxic drug
- Linkers can be broadly categorized as cleavable and Non-cleavable

Payload

- Cytotoxic payloads also called as “warhead” are highly potent drugs used in Antibody-Drug Conjugates (ADCs) to target and kill cancer cells

Mechanism of action:

1. **Targeting Specific Antigen**: The monoclonal antibody component of the ADC targets and bind to specific antigens that are overexpressed on the surface of cancer cells
2. **Internalization**: Entire ADC complex is internalized into the cancer cell through receptor-mediated endocytosis.
3. **Intracellular Release of the Cytotoxic Drug**: After internalization, ADCs are processed inside cancer cells, where the linker molecule connecting the antibody to the cytotoxic drug is degraded. This degradation, triggered by enzymatic cleavage or reduction, releases the cytotoxic drug.
4. **Cytotoxic Effect**: Cytotoxic drug exerts its toxic effects on the cancer cell. These effects can include DNA damage, disruption of cellular processes etc



REVIEW OF LITERATURE

ACS Publications
Most Trusted. Most Cited. Most Read.

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The Evolving Landscape of Antibody–Drug Conjugates: In Depth Analysis of Recent Research Progress

Janet M. Sasso, Rumiana Tenchov, Robert Bird, Kavita A. Iyer, Krittika Ralhan, Yacidzohara Rodriguez, and Qiongqiong Angela Zhou*

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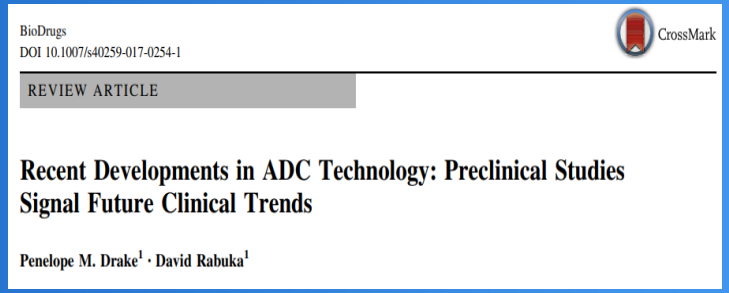
Review Article | Open access | Published: 22 March 2022

Antibody drug conjugate: the "biological missile" for targeted cancer therapy

Zhiwen Fu, Shijun Li, Sifei Han, Chen Shi & Yu Zhang

Signal Transduction and Targeted Therapy **7**, Article number: 93 (2022) | Cite this article

192k Accesses | **419** Citations | **171** Altmetric | Metrics



BioDrugs
DOI 10.1007/s40259-017-0254-1

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REVIEW ARTICLE

Recent Developments in ADC Technology: Preclinical Studies Signal Future Clinical Trends

Penelope M. Drake[1] · David Rabuka[1]

Methodology

- Research Question

What is the current landscape of ADCs in terms of drugs that are in clinical phases and those that have already been approved?

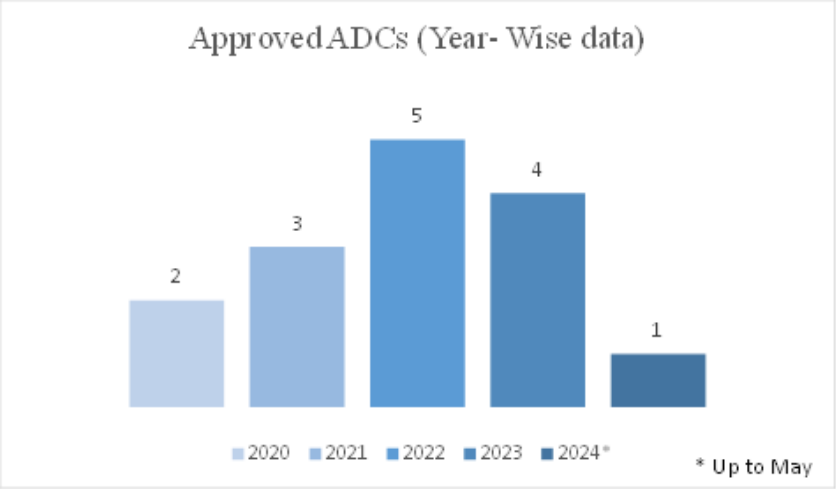
- Objectives:
  - To investigate approved ADC from 2020-2024
  - To assess the growth and increasing trend of ADCs across various therapy areas
  - To examine different Indication for which ADCs are approved
- Sampling Techniques

Convenience sampling is used to select literature from prominent databases such as NIH, PubMed, Scopus, ClinicalTrials.gov, Web of Science, and Google Scholar

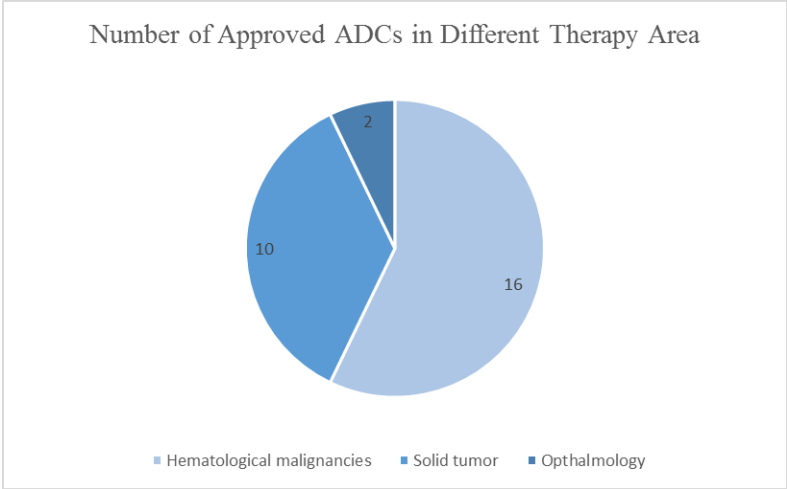
- Research Design

This study employs an observational study-based approach through retrospective literature review.

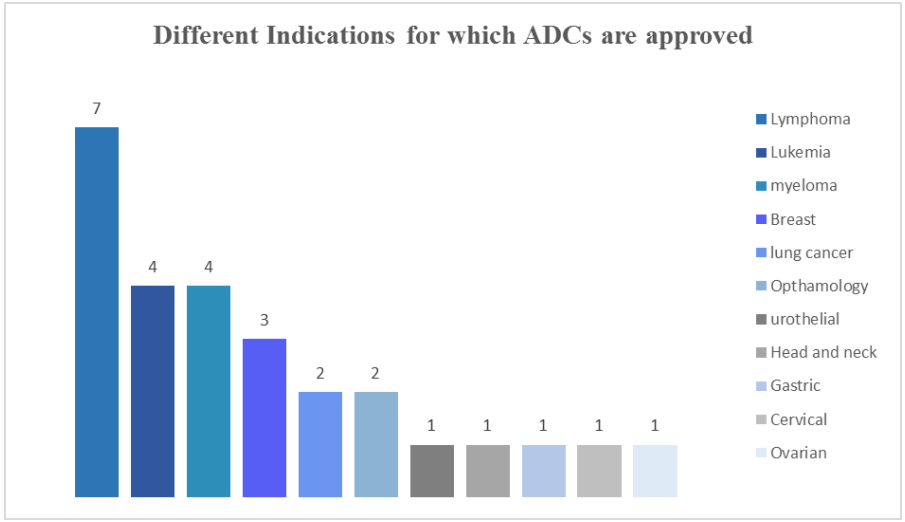
RESULTS AND DISCUSSION

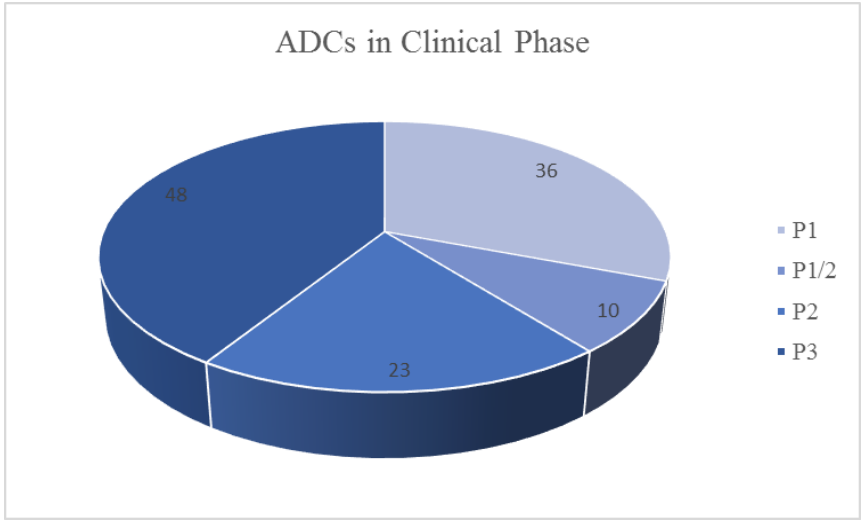


The bar chart shows the yearly number of antibody-drug conjugate (ADC) approvals from 2020 to 2024. Approvals increased from 2 in 2020 to 3 in 2021, peaking at 5 in 2022. In 2023, there were 4 approvals. As of May 2024, only 1 ADC has been approved, with more potentially to come later in the year.



The pie chart shows that 62% of approved ADCs target hematological malignancies, 28% target solid tumors, and 10% target ophthalmology, reflecting a focus on hematological tumors, ongoing efforts in solid tumors, and emerging use in ocular diseases and other indications.





The column chart shows the number of approved ADCs for various conditions. Lymphoma leads with 7 approvals, followed by leukemia and myeloma with 4 each. Breast cancer has 3 approvals. Urothelial cancer, lung cancer, and ophthalmology each have 2, while ovarian, head and neck, gastric, and cervical cancers each have 1 approved ADC.

The pie chart shows ADC development among 10 companies. Currently, 48 ADCs are in Phase 3 trials, and 46 are in early stages: 36 in Phase 1 and 10 in Phase 1/2. This indicates significant ongoing research and a strong focus on advancing ADC therapies.

LIMITATION OF STUDY

Temporal Limitation

The data on approved ADCs spans only five years (2020 to 2024), which may not fully capture long-term trends and developments.

Limited Scope of Research:

The study did not conduct extensive research into all aspects of ADCs, such as long-term safety profiles, resistance mechanisms, and cost-effectiveness.

Data Source Bias:

The reliance on available literature and data sources may introduce bias, as unpublished or ongoing studies were not considered.

CONCLUSION

- **Transformative Targeted Therapies:** ADCs combine antibodies, linkers, and cytotoxic payloads for precise tumor targeting and improved therapeutic efficacy. Advancements from first to third-generation ADCs enhance treatment outcomes and reduce side effects.
- **Robust Pipeline:** ADCs are in various stages of development, indicating potential expansion into non-oncological fields such as autoimmune diseases and dermatological conditions.
- **Emerging Technologies:** Innovations like Bi-specific T-cell Engagers (BiTE) and T-cell engaging bispecific antibodies (TiDE) promise to augment ADC efficacy, potentially revolutionizing treatment across various therapeutic domains.
- **Future Potential:** Continued interdisciplinary collaboration and rigorous investigation are crucial for fully realizing the therapeutic potential of ADCs and optimizing their clinical impact across diverse patient populations.


THANKYOU