Branding Science Group

Introduction to ADCs

Antibody drug conjugates (ADCs) form a promising class of targeted therapy in the field of oncology - here is everything you need to know about them

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What are Antibody-Drug Conjugates?

Antibody-drug conjugates, commonly known as ADCs, are a class of drugs that use monoclonal antibodies to deliver toxins to specific cells.

ADCs are currently exclusively used as a targeted therapy for managing and treating various types of cancer, although they are being tested for other disease areas such as HIV and blood disorders.

ADCs are popular for cancer treatment as they offer a targeted delivery of the drug to specific cancer cells, minimising the exposure of the drug to healthy cells in the body. The high specificity of ADCs therefore makes them an advantageous treatment option for cancer, as they can reduce the side effects associated with traditional chemotherapy.

13 ADCs have been approved to date

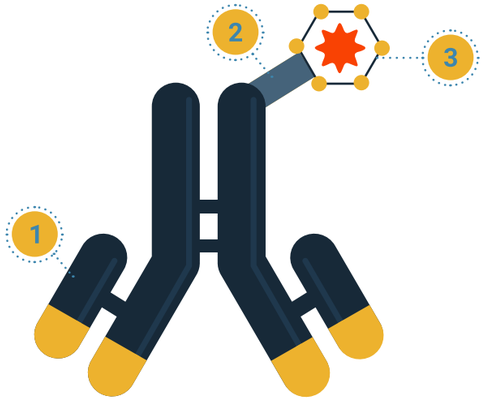
In the last twelve years, 13 oncology ADCs have been approved by the FDA for the treatment of blood cancer, breast cancer, lung cancer, gastric cancer, urothelial cancer, cervical cancer and ovarian cancer.

Company	ADC	Indication	Launch date
Seagen / Takeda	ADCETRIS	Hodgkin lymphoma / sALCL / CTCL	2011
Roche	Kadcyla	HER-2-positive breast cancer	2013
Pfizer	BESPONSA	Acute lymphoblastic leukaemia	2017
Pfizer	MYLOTARG	Acute myelogenous leukaemia	2017
AstraZeneca	LUMOXITI	Hairy cell leukaemia	2018
Daiichi Sankyo / AstraZeneca	ENHERTU	HER-2-positive breast cancer / Gastric cancer / NSCLC*	2019
Seagen / Astellas	PADCEV	Urothelial cancer	2019
Roche	POLIVY	Diffuse large B-cell lymphoma	2019
GSK	BLENREP	Multiple myeloma	2020
Gilead	TRODELVY	Triple-negative breast cancer	2020
Sobi / ADC Therapeutics	Zynlonta	Diffuse large B-cell lymphoma	2021
Seagen / Genmab	tivdak	Cervial cancer	2021
immunogen	ELAHERE	Ovarian cancer	2022

Recently approved: *Enhertu has recently been approved for the treatment of NSCLC in Japan, Israel and the EU

ADC system: a three-component structure

Most ADCs are comprised of three components: a monoclonal antibody, a cytotoxic payload (also called the cytotoxic molecule, toxin or drug) and a stable linker that conjugates the specific antibody to the payload. Moxetumomab pasudotox, sold under the brand name Lumoxiti, is the exception as it is a 'linker less' ADC, which can be referred to as an immunotoxin.

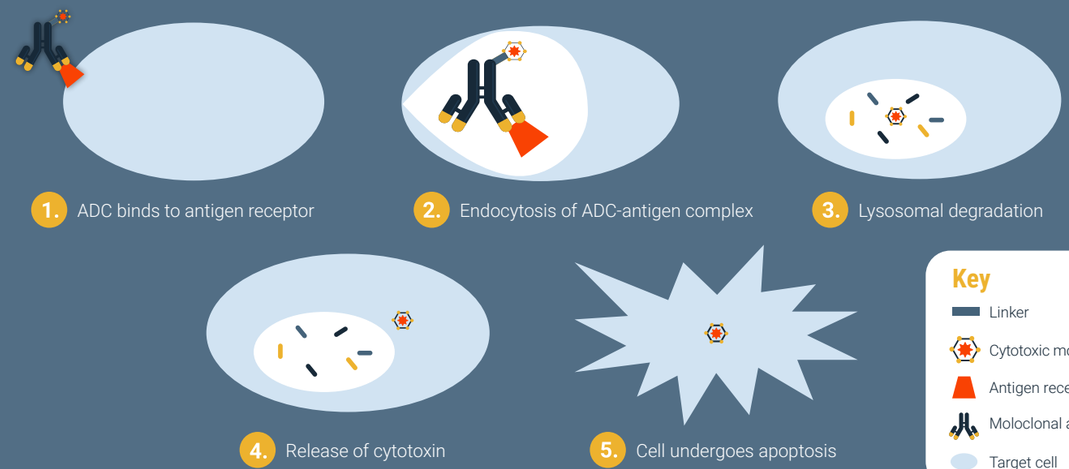


1. Antibody
2. Linker
3. Payload: cytotoxic molecule (toxin)

ADC's three-component structure

A targeted and highly specific mode of action

In ADCs, the monoclonal antibody acts as a 'trojan horse' in the delivery of the drug to the targeted cell, whilst the linker is a highly stable molecule that ensures the antibody and the payload stay linked in the bloodstream until uptake in the targeted cell.



All approved ADCs have the same broad mechanism of action:

1. After traveling through the bloodstream, the monoclonal antibody of the ADC binds to the antigen receptor on the surface of the targeted cell
2. Binding of the antibody to its antigen generates uptake of the ADC-antigen complex into the cell - this process is called endocytosis as the ADC-antigen complex enters the cell in a vesicle called the endosome
3. Once in the cell, the antibody and linker undergo degradation
4. During lysosomal degradation, the cytotoxic molecule is released from the endosome into the cell
5. The release of the drug into the cytoplasm kills the cell

Why are ADCs attractive to pharma companies?

In the past twelve years, ADCs have had significant success in revolutionising cancer treatment. ADCs' technological developments, together with their profit potential, have led to significant interest and investment in the space. These research and development investments are reflected in the number of current ADC clinical programmes. A handful of ADC blockbusters are paving the way for more therapies to come to market. Big pharma companies are competing in launching the next big ADC drug, creating a very competitive treatment and deal landscape.

1. Targeted and versatile

ADCs offer many advantages over traditional chemotherapy or other cancer treatments, including enhanced targeting of cancer cells, reduced toxicity and improved patient outcomes. Given their structure, ADCs show great potential for versatility as a wide range of monoclonal antibodies might be developed and further used to target different forms of cancers. The therapeutics market across oncology is increasingly growing, suggesting a strong market potential for ADCs. In addition to oncology, recent advancements in research suggest ADCs might be beneficial in treating other diseases including blood disorders, autoimmune, cardiovascular and bone diseases in the future.

2. High levels of intellectual property

Although ADCs' structure and mode of action remains the same across disease areas and indications, designing and developing ADCs is complex as originator antibodies are not always available and cytotoxic molecules can lead to serious side effects if not dosed appropriately. That element of complexity reduces the chance of other pharmaceutical companies creating biosimilars without significant R&D efforts, which provides ADCs with a high level of intellectual property protection. In addition to patent protection which provides companies with a period of exclusivity, intellectual property protection offers a significant competitive advantage, which makes ADCs attractive to develop. Lastly, the know-how process of developing an ADC complex provides a commercial advantage to companies who previously approved and launched ADCs.

3. Premium pricing

A further advantage to developing ADCs is the higher price pharmaceutical companies can charge for them, as their targeted delivery offers more advantages than traditional chemotherapy drugs. The vast amount of time and money invested in R&D, along with high manufacturing costs, also adds to ADCs' high price. Another advantage is that developers can keep ADC prices high for a longer period, as the risk of emerging biosimilars is low. This premium pricing allows companies to generate higher revenue and profits from ADCs compared to other traditional cancer drugs, which makes them more attractive.

4. Low-risk development

Although ADCs are complex, their consistent structure and mode of action offer a lower risk of development when compared to other oncology drugs. When developing them, pharmaceutical companies know what components they need and how they need to perform to ensure safety and efficiency. ADCs' mode of action is relatively simple and remains unchanged across therapy areas, meaning there are less unknowns in developing an ADC than developing a novel therapy from scratch. With pharmaceutical companies being attracted to risk-adverse options, this is one of the reasons ADCs have attracted more funding and investment than other oncology therapeutics.

5. Partnerships and licensing opportunities

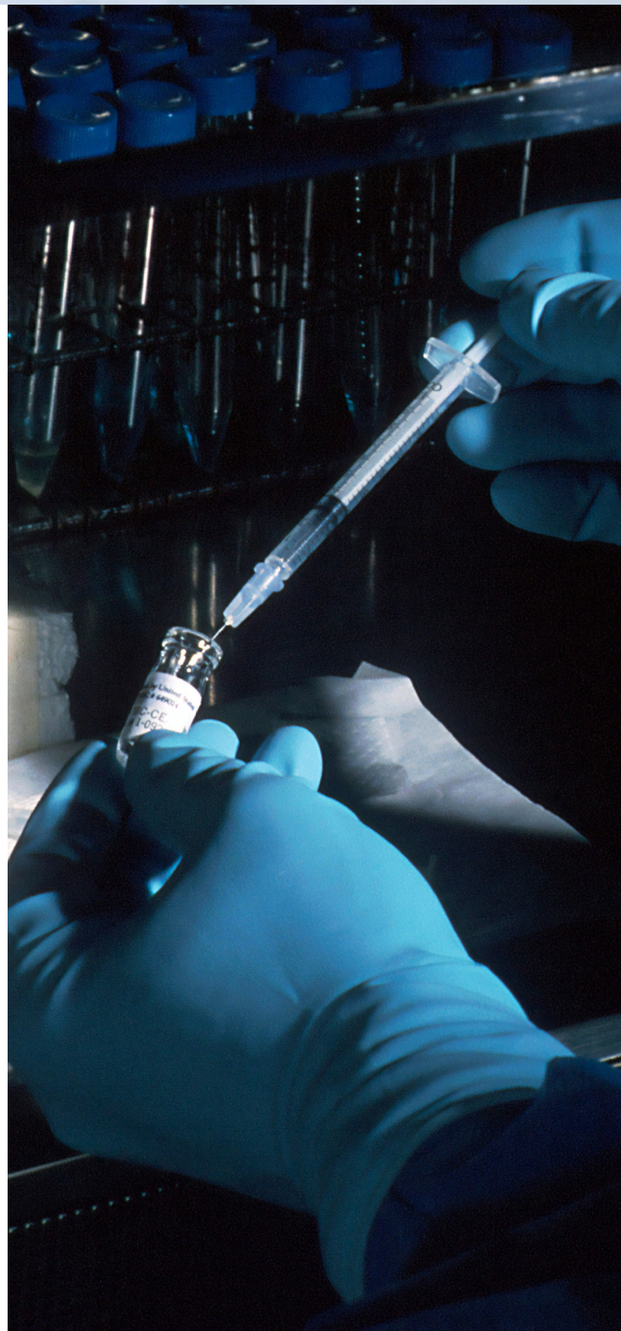
Small and large pharmaceutical companies continue to share their knowledge on ADC technologies by collaborating and partnering. Partnerships can help pharmaceutical companies gain expertise in specific areas, aid in finance development and increase the commercial potential of their drugs. Overall, ADCs are very promising, which makes them an attractive option for pharmaceutical companies looking to develop profitable drugs with a significant commercial potential.

What next for ADCs?

As a result of its attractiveness, the ADC market is growing rapidly with many deals and partnerships amongst small, midsized and large pharmaceutical companies. With many current ADCs in further clinical trials, new ADCs could rapidly be launched and market leaders might change. In addition, many approved ADCs are undergoing clinical trials to claim additional indications.

To gain valuable insights on the fast-evolving landscape and commercial appeal of antibody-drug conjugates, read our paper...

Read our additional paper:
ADCs The fuel for future growth



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